Regulatory Impact Analysis

42 CFR Part 73:
Select Biological Agents and Toxins
Interim Final Rule

Centers for Disease Control and Prevention
Department of Health and Human Services

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Executive Summary

This study examines the costs and benefits of the Centers for Disease Control's (CDC) interim final rule, which addresses requirements for entities that possess, use, or transfer select biological agents and toxins.[1] The analysis quantifies costs and impacts, as summarized later in this Executive Summary. Benefits have been addressed qualitatively and are summarized in the introductory text below.

ES.1 Introduction

Each of the agents placed on the select list poses a severe threat to human health. Existing biosafety procedures in the facilities using, storing, or transferring these select agents have made the likelihood of an unintentional outbreak low. However, Congress, in the Public Health and Bioterrorism Preparedness Act of 2002, directed CDC to promulgate rules to increase the security over such agents (including access controls and screening of personnel) and to establish a comprehensive and detailed national database of the location and characterization of such agents and the identities of those in possession of them.

The benefits to public health and safety from implementation of the rule are clear, although difficult to quantify. The benefits of the regulation result from the strengthened prevention that the rules provide against either accidental or intentional release of a biological agent or toxin. The cost of such an event in human life could be very high. An outbreak of one of the biological agents or toxins would require a complicated and expensive emergency response effort. This effort could include extensive public health measures, such as quarantine, preventative treatment and health testing for large numbers of potentially exposed persons, and extensive decontamination. Substantial costs could be incurred by hospitals and other medical facilities and institutions of government at all levels. An outbreak, or widespread fear of one, also would create significant secondary effects. It could disrupt business, transportation, and many other aspects of normal behavior, on both a short-term and potentially a long-term basis.

[1] The terms "select biological agents and toxins" and "select agents" are used interchangeably in this report.

The impacts resulting from the October 2001 anthrax attacks provide an example of the costs that the regulation will help to avoid. The anthrax attacks caused five fatalities and 17 illnesses, disrupted business and government activities, closed substantial parts of the postal service, and caused widespread apprehension and changes in behavior. Costs included more than $23 million to decontaminate one Senate office building, approximately $2 billion in revenues lost to the postal service, and as much as $3 billion in additional costs to the postal service for cleanup of contamination and procurement of mail-sanitizing equipment. Substantial costs due to lost productivity throughout the economy and from ongoing costs of the investigations into the incident are additional impacts.

The interim final rule will create a means of determining where select biological agents and toxins are located; ensure that their transfer, storage, and use can be tracked; provide for the screening of personnel with access to such agents; and require that entities in possession of such agents develop and implement effective means of biosafety and physical security. The benefit of these provisions is a reduced likelihood of either an accidental or intentional release of select biological agents and toxins and the consequent avoidance of costs associated with such a release.

ES.2 Affected Universe

At least 1,653 entities have indicated that they possess select agents. Of these, 1,167 entities are expected to fall under the purview of CDC/HHS (as opposed to USDA). Of the 1,167 entities expected to be of concern to CDC/HHS, only 817 are expected to register under the rule. The remaining 350 entities perform only diagnostic work and are expected to be exempt from many rule provisions, thereby avoiding most of the regulatory burden associated with the rule. The 817 entities that must register can be divided into four types, as shown below in Exhibit ES-1.

Exhibit ES-1
Summary Characterization of Affected Labs

Type of Entity	***Predominant Organizations***	***Estimated Number***	***Estimated Proportion***
Academic	Universities	285	35%
Commercial	Manufacturing Facilities	375	46%
Government	Federal and State Labs	98	12%
Private Non-Profit	Research Institutes	59	7%

These figures report the number of entities, where individual entities may operate multiple labs. For example, a major university is counted as one entity even if it

operates numerous distinct labs spanning multiple departments or principal investigators.

To protect facility staff as well as the public, labs using select agents already employ a variety of laboratory safety practices. In general, facilities are adhering to guidance in the *Biosafety in Microbiological and Biomedical Laboratories (BMBL), 4th Edition*, as applicable to their specific biosafety level category (e.g., BSL-2, BSL-3, BSL-4).[2]

There is wide variation in current security practices, although there is a correlation (as expected) between BSL levels and security levels. For example, BSL-3 labs tend to have more security than BSL-2 labs. Nevertheless, even for labs of the same type or BSL level, some variation exists. There also appears to be systematic variation across labs of different types. In general, this study finds that security is relatively stronger at federal labs, research institutes, and commercial labs; security practices at universities and state labs are more variable, but on average are less protective than the other types of facilities.

ES.3 Costs of the Rule

The study estimates the total, annualized cost of the rule at $40 million. Most of this cost will be incurred by affected labs. CDC as the implementing agency will incur somewhat less than $1 million dollars of the annualized total. Because the total annualized cost of the rule is less than $100 million, the rule does not meet the test for an economically significant rule under Executive Order 12866. (Nevertheless, CDC has determined that the rule qualifies as a significant rule for the reasons discussed in Section 5.1.)

The median annualized cost of the rule to non-exempt labs is estimated at $29,000, and the range of annualized facility costs is $9,000-$198,000. The average annualized facility cost for exempt clinical/diagnostic labs is estimated at less than $600.

The cost model is based on a “model facility” approach. That is, the study developed a number of model facilities (32 facilities) intended to be representative of the various laboratories that actually will be affected by the rule. The models, which are based on research described elsewhere in this report, are believed to reflect enough of the variation between labs to provide a reasonable basis for quantifying the costs of the rule.

[2] Biosafety levels range from BSL-1 through BSL-4, although BSL-2 represents the minimum level at which labs might reasonably work with limited quantities of certain select agents. Based on research conducted for this study, the analysis assumes that only a relatively small number of labs (49 labs, or 6 percent of the 817 expected to register) use safety practices that are inadequate for appropriate handling of select agents.

ES.4 Impacts

To determine whether firms that own affected lab facilities will be impacted to a significant degree by the rule, the study compares the annual revenue of appropriately-sized entities in the relevant industries (including non-profit entities, such as some universities and hospitals) to the rule's estimated annualized cost for the appropriate model facilities. Because the rule's cost to affected entities will be highest in the first year in which the rule is effective, this study also considers whether entities may face significant impacts in the first year, even if the annualized impacts are not significant. Entities are assumed not to incur significant impacts unless either or both of the following screening criteria are met:

- The entity's estimated ratio of annualized cost to revenue exceeds one percent.

- The entity's estimated ratio of first-year costs to revenue exceeds three percent.

Using these criteria,[3] affected entities – including small entities – are not expected to face significant impacts as a result of the rule.

ES.5 Key Assumptions

The analysis assumes that the minimum physical security measures that will be needed in order to comply with the rule are as follows:

- All select agent labs: (1) must have and use locked storage cabinets for select agents; (2) must have and use locks on all doors into areas where select agents are used or stored; and (3) must control the distribution of keys to select agent work and storage areas.

- All BSL-3 labs: (1) must use a card-key system to allow and log entrance into and exit from areas where select agents are used and stored; (2) must station an unarmed security guard at the entrance to each building or floor where select agents are used or stored during working hours; and (3) must use a guard or an intrusion detection system (e.g., motion detectors, sound detectors) during non-working hours.

[3] These criteria are intended to serve as screening-level indicators and may be overly sensitive for purposes of identifying economic impacts, as discussed in Section 3.6. Additional analysis would be required to determine whether firms meeting either of these conditions are likely to incur significant impacts as a result of the rule.

- All BSL-4 labs are assumed to have adequate physical security measures already in place to comply with the rule, although these labs may incur some other security-related costs.

ES.6 Required Regulatory Analyses

The rule has been examined in relation to various federal statutes and executive orders to determine whether additional regulatory analyses are required. As discussed in Section 5 of the report, no additional analyses are required beyond the analysis addressed above.

1. Introduction

In the Public Health and Bioterrorism Preparedness Act of 2002 Congress set three goals for the provisions pertaining to select biological agents and toxins:

(1) "to ensure the prompt reporting to the Federal government of possession of select agents;"

(2) "to increase the security over such agents (including access controls and screening of personnel);" and

(3) "to establish a comprehensive and detailed national database of the location and characterization of such agents and the identities of those in possession of them."

Congress delegated to the Centers for Disease Control (CDC) within the Department of Health and Human Services (HHS) and to the U.S. Department of Agriculture (USDA) the responsibility for preparing regulations to accomplish these goals. The costs and benefits of the CDC's interim final rule addressing requirements for entities that possess, use, or transfer select biological agents and toxins are the subject of this study.

The benefits to public health and safety from implementation of the standards mandated by Congress are clear, although difficult to quantify. Each of the agents placed on the select list poses a severe threat to human health. (Appendix 1 provides short descriptions of the select agents whose possession, use, and transfer are under the specific jurisdiction of the CDC, the "non-overlap" agents. The description of each agent indicates the parts of the world where the agent is endemic and its means of transmission, symptoms and estimated fatality rate, treatment, and potential for terrorist use.)

Select agents currently are subject to laboratory biosafety standards, commensurate with the risk that each individual agent poses to public health and safety. Congress now has added to these health and safety considerations the additional consideration that such agents could be used in domestic or international terrorism. The requirements for registration of possession enhance both biosafety and security. The new security requirements address directly the potential for the agents' use in acts of terror.

Because the biological agents and toxins whose possession, use, and transfer are regulated by this rule are extremely dangerous to human health, lapses in safety or security have the potential to inflict severe harm to the U.S. population. These agents and toxins share a number of threatening characteristics:

- Illnesses resulting from these agents and toxins are generally associated with high fatality rates. For example, some forms of anthrax and smallpox are associated with fatality rates of almost 100 percent, yersinia pestis (plague) up to 90 percent, and herpes B-virus up to 70 to 80 percent.

- Although the biological agents and toxins spread through a variety of modes, many of them can spread quickly throughout a population, resulting in sudden epidemics.

- Because a majority of these agents are rare and exotic, they are difficult for doctors to recognize, especially in the early phases. Delays may result in wider dissemination.

- An effective vaccine or treatment currently does not exist for many of these agents and toxins.

Biosafety procedures in the facilities using, storing, or transferring these select agents have made the likelihood of an unintentional outbreak low. However, as Congress has recognized, the agents could be released either accidentally or intentionally as an act of bioterrorism, and in either case the cost of such an event in human life could be high. The public health and social costs of an accidental release would depend upon where and how the agent was introduced to the population. In the event of an intentional release, however, these agents and toxins might be dispersed strategically to inflict maximal damage and hinder public health response. The delayed onset (incubation period) of many of the contagious biological agents, and the almost immediate onset of the toxins, provide different, but in both cases troubling, possibilities for bioterrorism.

An outbreak of one of the biological agents or toxins would require a complicated and expensive emergency response effort. This effort could include extensive public health measures, such as quarantine, preventative treatment and health testing for large numbers of potentially exposed persons, and extensive decontamination. Substantial costs could be incurred by hospitals and other medical facilities and institutions of government at all levels.

An outbreak, or widespread fear of one, also would create significant secondary effects. It could disrupt business, transportation, and many other aspects of normal behavior, on both a short-term and potentially a long-term basis.

The effects of the October 2001 anthrax attacks provide a recent example of the public health costs and social impacts of an intentional release of a biological agent. The human health impacts were relatively low, with five fatalities and 17 illnesses. In addition, however, the anthrax releases disrupted business and government activities, closed substantial parts of the postal service, and caused widespread apprehension and changes in behavior on the part of a large portion

of the population. Decontamination of one Senate office building cost more than $23 million. Mail to many government agencies was quarantined and severely delayed. The postal service lost an estimated $2 billion in revenues and may spend as much as $3 billion for cleanup of contamination and procurement of mail-sanitizing equipment. Substantial costs of lost productivity throughout the economy and ongoing costs of the investigations into the incident are additional impacts.

The interim final rule will create a means of determining where select biological agents and toxins are located; ensure that their transfer, storage, and use can be tracked; provide for the screening of personnel with access to such agents; and require that entities in possession of such agents develop and implement effective means of biosafety and physical security. The potential benefit of these provisions is a reduced likelihood of either an accidental or intentional release of select biological agents and toxins and the consequent avoidance of costs associated with such a release.

2. Affected Universe

This section characterizes the universe of laboratories expected to be affected by the rule. Except as noted, the section is based on two primary information sources. The first set of information consists of summary statistics drawn from required notifications from entities possessing select agents.[4] (Entities in possession of select agents were required to provide notification to CDC/HHS and USDA by the *Public Health Security and Bioterrorism Preparedness and Response Act of 2002.*) The notification data provided quantitative estimates of affected labs, along with some rudimentary classification of labs by type (i.e., university, government, commercial, research institute) and by the type of work performed (e.g., diagnostic work, vaccine development, research, production, teaching, storage only). The second set of information was obtained through a limited number of telephone interviews with affected labs. These interviews (which were conducted as part of this study) were designed to provide general information on facility characteristics, focusing in particular on characteristics related to safety and security.[5]

2.1 Overview

In response to the notification requirements noted in the preceding paragraph, 1,653 entities indicated that they possess select agents.[6] Of these, 1,167 entities are expected to fall under the purview of CDC/HHS (i.e., for purposes of registration, exemption, etc.) based on the category of their select agents and/or on the nature of the activities these entities conduct. The remaining entities will fall under the oversight of USDA. Individual entities may operate multiple labs. For example, a major university is counted as one entity even if it operates numerous distinct labs spanning multiple departments or principal investigators.

Of the 1,167 entities expected to be of concern to CDC/HHS, only 817 are expected to register under the rule. The remaining 350 entities perform only diagnostic work and are presumed exempt from most of the rule.[7] The 817 entities that must register can be divided into four types:

[4] This study did not have access to any lab-specific survey data.

[5] Interviews were designed to identify differences between various categories of labs (e.g., large versus small, government versus commercial) as opposed to differences relating to the use of a given select agent versus a different select agent. For security reasons, labs were not asked to identify their select agents.

[6] Entity totals are based on positive notifications as of October 18, 2002.

[7] The rule's exemption provisions (specifically, the exemption for entities that possess, use, or transfer select agents only as contained in specimens presented for diagnosis, verification, or proficiency testing) require these entities to comply with certain transfer and notification requirements and to destroy or transfer select agents within specified time periods, but the entities need not comply with other provisions of the rule.

- Academic: 285 (approximately 35 percent);
- Commercial: 375 (approximately 46 percent);
- Government: 98 (approximately 12 percent); and
- Private non-profit: 59 (approximately 7 percent).

These four category groupings are consistent with the forms that were used in connection with the notification requirements (see discussion above). This study, however, references two of the above groupings using slightly different terminology. Specifically, "academic" labs are referred to as "university" labs, as universities are the predominant type of academic institution that uses select agents. In addition, "private non-profit" labs are referenced as "research institutes," as the latter name is slightly more descriptive. For purposes of this report, the two sets of terms (i.e., "academic" versus "university," and "private non-profit" versus "research institute") may be used interchangeably.

2.2 General Facility Characteristics

Facilities that handle select agents exhibit a wide range of characteristics. In this report, they are categorized primarily by type of institution (e.g., federal, state, commercial, research institute, and university) and by Biosafety Level (e.g., BSL-2 and BSL-3). Within the parameters of these two categories, this section identifies and examines some general facility characteristics for facilities that handle select agents.

2.2.1 Employees Handling Select Agents

In general, facilities limit access to select agents to a far smaller population than their overall workforce. In most cases, this smaller population is composed of authorized scientific staff.

The number of employees directly handling select agents typically ranges from approximately three individuals at smaller commercial and state facilities to more than one hundred researchers at some large universities. Although this range is very broad, certain types of facilities have more employees authorized to work directly with select agents. On average, commercial facilities authorize approximately 12 individuals to work with select agents. Similarly, at state facilities the average number of authorized employees is estimated at about 15. Authorized populations at research institutes and at federal facilities are larger, with approximately 25 employees handling select agents on average. Universities have the largest staff directly working with select agents, averaging almost 40 authorized persons per facility.

2.2.2 Employees with Access to Areas Containing Select Agents

In addition to those individuals who are authorized to handle select agents, other employees also may have access to the rooms in which select agents are stored. This population includes technical staff working in the same space, as well as janitors and maintenance staff. At BSL-2 labs, these additional persons may be numerous (e.g., up to 50-75 additional employees). Access to labs is generally more limited (e.g., an average of 9 additional employees) when the facility contains BSL-3 labs handling select agents. Interestingly, at universities, where the population authorized to handle select agents is the largest, select agent labs are accessible to few others beyond authorized staff (an average of 8). This may reflect the fact that many universities (66 percent) have both BSL-2 and BSL-3 labs. A small minority of labs does not systematically exclude persons who have no specific reason to be in the select agent areas.

2.2.3 Staff Turnover

The turnover rate of employees at affected facilities' is estimated at 10 percent of employees per year. When broken down further, state facilities exhibit the lowest employee turnover rate (just over 5 percent), while universities exhibit the highest employee turnover rate (just over 13 percent). University labs are often staffed with graduate and post-doctoral students, individuals who are regularly replaced with new students.

2.2.4 Location of Select Agents

Most facilities store and use their select agents in the same spaces. Many facilities do so with the express purpose of limiting the transfer of select agents from one space to another. In general, labs handling select agents are concentrated in a single building if not also on a single floor of that building. The exception to this rule would be at larger universities, where labs handling select agents are spread out across more than one building (as many as twelve different buildings at one university).

At most facilities that house all select agent labs within a single building, the majority of rooms for storage and use of select agents are gathered together on a single floor. The number of rooms for storage and use of select agents varies a great deal from facility to facility, but most facilities handle select agents in more than one room. Commercial facilities, for example, have an average of 4-5 rooms for the storage and use of select agents. Universities and research institutes use the most rooms for select agents, with averages of 10 and 15, respectively, and maximums of 20 and 28, respectively.

It is common for facilities to store and use their select agents in the same space (approximately 75 percent). It is not uncommon, however, for additional separate rooms to be used. One typical example would be a research institute where a BSL-3 lab complex includes 3 rooms for storage of select agents and four additional rooms for working with the select agents.

2.2.5 Categories of Select Agents

The select agent list is categorized into the following five types of agents: toxins; bacteria; viruses; nucleic acids, and fungi. Based on available information, smaller facilities use only one type of select agent. With use of only one type of select agent limited to smaller facilities (mainly BSL-2 labs), most facilities (approximately two-thirds) handle at least two types of agents, and approximately half handle more than two types of select agents as well. Finally, about 20 percent of all facilities handle all four types of agents; these high volume facilities can be commercial facilities, research institutes, and universities.

Half of all facilities handle toxins, viruses, and/or nucleic acids. Over 70 percent of facilities are handling bacteria. Although BSL-2 labs handle each of the four types of select agents, they handle a larger percentage of toxins and bacteria than viruses and nucleic acids. Most BSL-2/3 labs are handling bacteria (90 percent) and viruses (70 percent), at least half also handle toxins and nucleic acids.

The *number* of select agents used by labs ranges from one to more than 20. Approximately 30 percent of labs use three or fewer agents, while about 70 percent of facilities handle four or more agents. About eight percent of all facilities handle more than 20 agents.

2.2.6 Frequency of Use

The handling of select agents at facilities differs from one type of institution to another. In general, half of all facilities are using their select agents on a daily basis, while the other half works with their select agents much less frequently.

Commercial facilities, many of which manufacture vaccines, can be broken into two groups. Smaller commercial facilities typically handle select agents on a weekly basis, whereas larger commercial facilities handle select agents on a daily basis. At many universities (approximately two-thirds), select agents are being handled on a daily basis. This is largely a result of both the large number of select agent labs found at universities as well as the high average number of employees authorized to work with select agents. At research institutes, handling of select agents reflects the facility size, with smaller institutions working with agents on a weekly or monthly basis and larger institutes doing so daily. State facilities work with select agents 3-4 times per week, on average.

At facilities that handle both toxins and other select agents, toxins are in use at least as much as the other agents, if not more often.

2.2.7 Shipping Select Agents

Most facilities that handle select agents (approximately 75 percent) also send or receive select agents. Slightly more than half of these facilities are only receiving select agents with most of the rest both sending and receiving.

Facilities transfer select agents for a variety of reasons, from acquiring specific strains for developing antibodies to collaboration with other researchers. In fact, over half of facilities sending and/or receiving select agents are doing so for scientific collaboration; much of this collaboration is with the CDC. An estimated four-fifths of commercial and state facilities are sending and receiving select agents. Among state facilities, collaboration with the CDC is the only reason that they are currently sending and receiving select agents. Approximately half of universities are sending and receiving select agents. Among facilities that currently do not send or receive select agents, most have transferred select agents at some point in their institutional history.

Although some facilities are shipping select agents at least 12 times per year (approximately 30 percent), about half of the facilities that transfer select agents do so less than five times annually. When sending or receiving select agents, the vast majority of facilities (at least 75 percent) use Federal Express (shipping methods for other labs were unknown or not specified).

2.3 Safety Practices

To protect facility staff as well as the public, facilities using select agents employ a variety of laboratory safety practices. In general, facilities are using the *Biosafety in Microbiological and Biomedical Laboratories (BMBL), 4th Edition* for guidance. This section also addresses other safety related practices, including decontamination and disposal practices, inventory practices, training, and safety plans.

2.3.1 Use of the BMBL

The vast majority of facilities that have labs with select agents are aware of the BMBL 4th Edition. The facilities know their Biosafety Level (BSL) category, and they follow the standards associated with their safety level as outlined in the BMBL.

About one-third of facilities have multiple lab rooms where some proportion of labs operate at BSL-2 and some operate at BSL-3, depending upon the category of select agents that are being used in the respective lab rooms. An estimated 38 percent of facilities solely have labs with select agents that operate at BSL-2. Approximately 30 percent of facilities exclusively have labs with select agents that operate at BSL-3. Only four facilities in the United States are believed to have labs with select agents that operate at BSL-4.

2.3.2 Training

Most labs (approximately 70 percent) have a training program in place that addresses the safety of staff that are in proximity to or handling select agents. Of the remaining facilities (that do not have a standard safety training program in place), some of them train people on the job as necessary for the employee to learn some skills or improve his or her proficiency. All commercial facilities have a standardized safety training program in place – at the very least for the technical staff that work in the labs.

Facilities reported a range of 4 to 40 hours to develop a safety training program, but the typical amount of time is approximately 20 hours. Updating the training usually requires about 4 or 5 hours per year. The training can take anywhere from 1 to 40 hours to administer, depending on the facility, but the average is about 10 hours. If refresher training is required, it is usually given annually.

Specific elements of the training programs vary, but most of the safety training programs that deal with select agents are only administered to the technical staff that will be handling the materials. In some instances, the facility may train everyone who works in the area where the select agents are being handled, but that is infrequent. Some training programs consist of a portion of general training that is given to all laboratory staff, followed by an additional portion that is specific to the materials that a person will handle.

Of those facilities with training programs in place, more than half of them train non-technical staff with respect to the safety of select agents. Often the training of non-technical staff includes everyone who is employed at the facility, but it may include only those who are permitted to enter the lab area that contains the agents (including maintenance workers). Overall, the training program for the non-technical staff is less detailed and takes less time, as they may only learn basic safety information about the agents or the general procedures of the facility's emergency plan.

2.3.3 Inventory Records

The vast majority of facilities (85 percent) have a system in place to record and monitor the inventory of select agents. Facilities without a system in place are

limited to a subset of BSL-2 labs. Of those facilities with an inventory system, the simplest and most common (90 percent) method reported requires the lab personnel receiving or using the select agent to record information in a log book using an ink pen. In general, the labs are recording which material is received or used, the amount, the date, and person's name and/or initials. At a minimum, inventory is monitored so that a facility knows when to order or grow more of a material. A more detailed inventory system might include information such as why the material is being used or data on materials being transferred from room to room. More sophisticated methods of monitoring inventory log the information into a computer file, usually in an Excel spreadsheet that is part of a centralized database. This method allows facilities with more than one lab room to store all the information in one place. Sometimes a computerized system is used in addition to the handwritten log book. For example, one sophisticated system requires the lab personnel to scan the bar codes of the vial being used in addition to recording details (such as reason for use, date, time, person's name) in a handwritten log book. Not surprisingly, the computerized logging systems were only found to be in place at facilities that have BSL-3 labs.

To prevent the records from being incorrectly recorded, some labs have two people verify the entry. Other labs lock the log book in a drawer or in the lab director's office, while other labs simply leave the log book in the lab so that everyone who works in the lab has access to the log book at all times. If a computer system is used, usually only select people have access to the files, such as the lab director or the Principal Investigator (PI) of the lab. In most instances, facilities keep the log books and computer files indefinitely.

2.3.4 Safety Plan

The vast majority of labs (over 90 percent) have a documented safety plan in place. This is consistent with the BMBL standards, which require a safety plan. Only some state and university facilities are assumed to not have a safety plan.

The amount of time needed by labs to develop the safety plan varies among facilities. Total hours spent developing a safety plan for all a facility's lab rooms ranged from 40 hours to 2,000 hours, with an average of approximately 540 hours. In an attempt to understand the time required to develop safety plans relative to the size of a lab, the total hours that a facility spends developing a safety plan was correlated to the number of lab rooms at that facility. The number of hours required to develop a plan ranged from 14 hours per lab room to 107 hours per lab room, with the average at about 50 hours per lab room.

The total number of hours that a facility spends updating the plan for all the facility's lab rooms ranges from 4 hours to 320 hours per year, with the average at around 50 hours per year. This equates to a range of 0.25 hours per lab room to 70 hours per lab room, with the average at about 10 hours per lab room.

To develop and maintain a safety plan, facilities enlist the help of various technical staff such as the Responsible Official (RO), safety engineer, security officer, biosafety officer, lab supervisor, lab director, and the principal investigator of a lab. The staff members at universities are usually a part of the Environmental Health and Safety department, while commercial facilities are likely to form Biosafety Committees.

2.3.5 Disposal Practices

Most or all facilities dispose of select agents. Frequency of disposal of select agents ranges from once per day to once or twice per year. The predominant method of disposal is autoclaving (81 percent). Other common methods include chemical disinfectant (or deactivation) and incineration. Of the labs that use incineration, approximately half of them send the material to an offsite facility and the other half conduct the incineration onsite. Most labs use a combination of methods depending upon the select agent that is being disposed. For example, one lab might use autoclaving for one agent and incineration for a different one. Alternatively, an agent might be chemically deactivated and then autoclaved.

2.3.6 Decontamination Practices

All facilities decontaminate their lab rooms, as called for by the BMBL requirements. Although most labs conduct a routine decontamination process that occurs at the end of every day during which work was performed in the lab, some labs also have various levels of non-routine decontamination that occur weekly, monthly, and/or yearly. The most popular method of decontamination is autoclaving (over 75 percent), then chemical disinfection (or deactivation) (over 70 percent). Fumigation (non-routine) and thermal inactivation are used infrequently.

2.4 Security Practices

Facilities with select agents employ various security measures to ensure the safety of their employees and the public. The most important feature of a security system, outlined in Section 2.4.4, is controlling access to the select agents by using a mechanical device (e.g., card key system or key locks). Labs may employ a device at one of four different locations that lead to the area where select agents are located (building, floor, lab room, and container). The vast majority of facilities that have at least one lab at BSL-3 maintain access controls at three of these levels, one of which is always the container that holds the select agent. BSL-3 facilities are also likely to use card key systems. Facilities that only have labs at BSL-2 employ access controls at two of these locations (the combination of which may vary by facility).

The remaining sections discuss the findings related to additional security features, such as security plans, background checks, identification badges, and other security features such as guards or security cameras.

2.4.1 Security Plan

More than half of all facilities have a documented security plan in place (slightly more than 60 percent). Of those with a plan in place, almost all consulted with at least one expert outside of the facility, such as the local police department, security agencies, former Federal agents, architects with experience in building secure facilities, and Federal agencies such as the Centers for Disease Control or the Department of Defense.

2.4.2 Background Checks

Although fewer than half of labs conduct background checks, nearly all of those owned by research institutes and commercial facilities (approximately 80 percent) conduct background checks on employees who have authorized access to select agents. Specific elements of the background checks vary by organization, but at a minimum most include basic criminal background checks. Other, less frequent types of background checks include government secret clearance reviews (almost 20 percent) and credit checks (in addition to the criminal background check). Background checks are much less common at state and university facilities (less than 20 percent), but when conducted typically include only criminal background checks.

2.4.3 Identification (Badges)

Approximately half of facilities require identification badges to enter either the facility grounds or a building containing select agents. Of those facilities requiring badges, the receptionist or guard visually verifies each person prior to entry. In some instances, facilities have trained the employees to question anyone inside the building who is not wearing a badge.

2.4.4 Mechanical Access Controls (Locks)

Facilities use access control devices at a variety of locations: gate at the perimeter of the facility's property; building; floor; laboratory; and select agent storage container. Control devices include card key, electronic lock, infrared lock, and key lock. Generally, facilities lock fewer access points during normal business hours (e.g., building entrances unlocked; lab doors unlocked). The number of locations at which access is controlled varies by facility, but in general facilities with only BSL-2 labs have two levels at which access to the select

agents is controlled, and facilities with at least one BSL-3 lab have three levels at which access is controlled.

Entrance to Facility Grounds

Most facilities do not maintain access control at the perimeter of the property. An atypical example, one facility is surrounded by an alarmed barbed wire fence, and a guard controls access at the gate by visually verifying picture identification badges of all employees (visitors may only enter with an employee).

Building

During business hours, many facilities have unlocked main entrances to the buildings where the select agents are located. When the building is open to the public, there is usually a receptionist or guard sitting at the entrance, although that person may not be required to conduct any sort of security measure such as checking identification badges. At all facilities, buildings are locked after business hours.

Floor

Overall, most facilities (approximately 70 percent) employ some form of access control to the floor that leads to the lab area where the select agents are located. The vast majority of floor level access controls are card key access devices (approximately 85 percent).

Lab Level

At the lab level, almost all facilities employ access control devices (approximately 75 percent). Approximately half use key locks, and most of the rest use card key systems. Universities are among the facilities that use only key lock systems at laboratory doors.

Container Level

The majority of facilities use container-level access controls for select agents (approximately 75 percent). For example, a freezer storing the select agents has a key lock, or a metal lock box is stored in a refrigerator. All facilities reported that the BSL-select agents are being locked at this level.

Infrequently, a facility goes beyond having one lock at the container level. For example, one facility employs both a card key and key lock in order for a person to access the select agent. An even more advanced system requires a person to swipe a card key and enter a waiting area that is separated from the select agent area by unbreakable glass. While standing in that area, the person must be

visually identified via a camera and then swipe another card keypad before entering the room with the agents.

2.4.5 Other Security Features

2.4.5.1 Use of Guards

Overall, most facilities employ at least one guard (approximately 70 percent). At slightly more than half of these facilities, guards are located at the main entrance of a building that contains select agents, while the remainder are generally patrolling the building hallways or the facility property. Some facilities that do not maintain guards have a receptionist at the main building entrance who is able to contact authorities if necessary.

At those facilities that have guards, approximately half of the guards are armed. Commercial facilities generally do not use armed guards.

Most guards are located at a fixed position such as a building entrance or facility main gate entrance. Alternatively, guards patrol the interior and/or exterior grounds of the building that contains the select agents. Research institutes and universities generally rely upon patrolling guards only. Commercial and state facilities position guards at fixed locations or use patrolling guards at roughly equal frequencies.

2.4.5.2 Logging Access to Areas with Select Agents

More than half of all facilities use handwritten log books (approximately 60 percent), although their purposes vary by facility. Of those that use log books, nearly half require employees to log in and out at either the building or lab entrance where select agents are located. Some facilities only require log books for employees working in BSL-3 labs, while other facilities only require that the employees use the log books after hours (e.g., from 7:00 P.M. to 6:00 A.M.). At some facilities, visitors are the only people required to use the log book (approximately 30 percent).

Many facilities (approximately 70 percent) use a card key system for access to at least one point of entry (building, floor, lab room). At the majority of these, the card key system automatically logs access information (e.g., who, when, and where a card was used). At a relatively few facilities, employees must scan their card key when exiting specific areas where access is limited (e.g., where the select agents are used or stored).

2.4.5.3 Alarm Systems

Many lab facilities employ an alarm system (approximately 60 percent), although alarms are much less common at state and university facilities. Although the type of system varies by facility, commercial facilities and research institutes tend to use alarm systems that detect unauthorized access to specific entry points and or perimeter fences. Other alarm systems are remotely monitored by security companies that contact facility representatives and local area police when necessary.

2.4.5.4 Security Cameras

Approximately half of all facilities use security cameras. Almost all of the facilities with security cameras also have an alarm system in place. Security cameras are standard at research institutes, while universities use cameras much less frequently than other facility types (approximately 15 percent).

Security cameras are located at various facility entry points ranging from building entrances, to hallways leading to select agent labs, to entry points into the lab. In general, the security cameras are monitored by a guard, the activities are recorded, and tapes are stored indefinitely.

3. Methodology

This section describes the study's methodology for quantifying the costs of the rule to affected entities (including labs and CDC) and for evaluating the economic impact of the costs on labs. Section 3.1 provides an overview of the methodology, and additional details are provided in Sections 3.2-3.6. Results of the analysis are presented in Section 4.

3.1 Overview

The analysis evaluates the costs and impacts of the rule based on a detailed assessment of the rule's various provisions and of what affected entities will need to do in response to these provisions. Section 3.2 summarizes those provisions of the rule that are expected to result in costs to affected entities.

The cost model is based on a "model facility" approach. That is, the study developed a number of model facilities (32 facilities) intended to be representative of the various laboratories that actually will be affected by the rule. The models, which are based on research described elsewhere in this report, are believed to reflect enough of the variation between labs to provide a reasonable basis for quantifying the costs of the rule. These model facilities are described in more detail in Section 3.3.

For each model facility, the cost model calculates each of the costs that the facility will incur to alter its facility or practices as needed to comply with each provision of the rule. Some costs are one-time costs, some occur periodically (e.g., every five years, whenever certain employees are hired), and some occur annually. For a 20-year timeframe, the cost model assigns appropriate costs to each year, calculates the net present value, and then calculates a level annualized cost.[8] This results in a total annualized cost for each model facility. The model facility costs are then scaled to a national aggregate annualized cost based on the estimated distribution of labs across the various model facility categories. Section 3.4 presents additional information regarding these steps, and Section 3.5 identifies some additional assumptions employed in the analysis.

The study considers the cost impacts of the rule, including impacts on small entities, by comparing the rule's cost for a given model facility to the annual revenue for the various types of entities that own affected labs of that model type. Further information on the impact analysis is presented in Section 3.6.

[8] All calculations involving net present value or annualization assume a seven percent discount rate.

3.2 Identify Required Activities

Costs associated with the rulemaking are those that must be incurred subsequent to the rule that are not incurred in the baseline.

As a first step in identifying these costs, this study identifies all of the provisions in the rule that will or may require action on the part of affected entities. It also identifies existing rules or standardized practices (such as those called for in the BMBL) that call for or require the same or similar actions from the same affected entities. Exhibit 3-1 summarizes the results of this first step. This information was used to help focus the research described in Section 2, to determine the baseline practices at model facilities, and to determine which incremental activities must be included as part of the analysis.

3.3 Model Facilities

To capture the diverse characteristics of laboratories affected by the rulemaking, the analysis identified and analyzed 32 distinct "model" facilities. The model facilities are intended, in the aggregate, to be representative of the various laboratories that actually will be affected by the rule, and to provide a reasonable basis for quantifying the costs of the rule. The models are based on research and assumptions described elsewhere in this report.

All but one of the 32 model facilities reflect different combinations of the following three characteristics:

- Facility Type. This characteristic specifies the nature of the entity handling the select agents. Five types are modeled:

  - Federal
  - State
  - Commercial
  - Research Institute
  - University

- Biosafety Level. Industry standard practices, such as those described in the BMBL, are the norm among labs that work with select agents. These "BSL" levels range from 1 through 4, although BSL-2 represents the minimum level at which labs might reasonably work with limited quantities of certain select agents. The biosafety levels represented in the models include the following:

Exhibit 3-1
Summary of New Requirements Resulting in Costs to Affected Entities

New Rule Requirement	Precedents in Existing Rules	Affected Entities
LABS		
73 Labs must familiarize themselves with the rules		All
73.6 Exemptions from requirements under this part		
(a)(2) Immediately report to CDC (via telephone, fax, or email) upon identification of select agents specified under this part		Exempt clinical and diagnostic labs
(a)(5) Transfer or destroy agents used for diagnosis or verification within 7 days after identification		Exempt clinical and diagnostic labs
(a)(6) Transfer or destroy agents used for proficiency testing within 90 days after receipt		Exempt clinical and diagnostic labs
(a)(7) Submit to CDC Form 0.1318 within 7 days of a transfer or destruction and maintain for 3 years		Exempt clinical and diagnostic labs
(c) Submit to CDC (Form 0.1317) an application to apply for an exemption (authorized investigations). The applicant must notify CDC when an authorization for an investigation no longer exists.		Individual labs on a case-by-case basis
(d) Submit to CDC (Form 0.1317) an application to apply for an exemption due to public health emergency		Individual labs on a case-by-case basis
73.7 Registration (Note: Registration under 42 CFR 72.6(a) is not assumed to be equivalent)		
(b)(1) Obtain registration application number from CDC before applying for approval		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(b)(2) Submit CDC Form 0.1319 as specified in the application package		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d) Notify CDC in writing if a change occurs to the latest info submitted (e.g., notification of list of individuals approved, change in area of work, or change in protocol or objective of studies)		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d) Submit application to amend certificate of registration if necessary (e.g., to add agents)		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(g) Submit new application to re-apply for registration when necessary (registrations are valid up to 3 years)		All non-exempt labs that possess, use, or transfer select biological agents and toxins

Exhibit 3-1
Summary of New Requirements Resulting in Costs to Affected Entities

(h) Notify CDC in writing at least 5 business days before destroying select agents, if the destruction results in discontinuation of activities covered by the certificate of registration		All non-exempt labs that possess, use, or transfer select biological agents and toxins
73.8 Security Risk Assessments		
(c) Submit to the Attorney General for a clearance the information requested at [web address]	Note: BMBL Appendix F states that background checks may be appropriate	All non-exempt labs that possess, use, or transfer select biological agents and toxins except Federal, State, or local government agencies
(f) Must re-apply for clearance at least every 5 years		All non-exempt labs that possess, use, or transfer select biological agents and toxins except Federal, State, or local government agencies
(g) Submit a request in writing for an expedited clearance review		Individual labs on a case-by-case basis
73.10 Safety		
(a) Develop and implement a safety plan that meets the requirements under this part	BMBL, p.8; OSHA Toxins Rule - Chemical Hygiene Plan required per 1910.1450(f)(4)	All non-exempt labs that possess, use, or transfer select biological agents and toxins
(b) R.O. or designee must conduct regular inspection of the laboratory where select biological agents and toxins are stored or used to ensure compliance with the safety plan (at least annually)		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(b) The results of these inspections must be documented		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(b) Any deficiencies identified during inspections must be corrected		All non-exempt labs that possess, use, or transfer select biological agents and toxins
73.11 Security		
(a) Develop and implement a (documented) security plan		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(b) The security plan must include the components specified under this part		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(c) Review the security plan at least annually and after any incident		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d) With respect to the select agent areas, the entity must adhere to the following security requirements:		All non-exempt labs that possess, use, or transfer select biological agents and toxins

Exhibit 3-1
Summary of New Requirements Resulting in Costs to Affected Entities

(d)(1) *Allow unescorted access only to individuals who are approved and are performing a specifically authorized function during hours required to perform defined job*	BMBL, p.225	All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d)(2) *Allow unapproved individuals to conduct routine non-lab functions only when escorted and continually monitored by approved individuals*		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d)(3) *Provide controlled access to storage containers where select biological agents and toxins are stored by requiring the containers be locked (e.g., card keys, lock boxes) when they are not in the direct view of approved staff, and by other measures as needed such as video surveillance*		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d)(4) *Require inspection of all packages before being brought into the area*		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d)(5) *Establish protocols for intra-entity transfers that include supervision of an approved individual*		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d)(6) *Ensure each approved person's access means (keys, passwords, combinations) are not used by any other person*		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d)(7) Each individual with authorized access to select biological agents and toxins must report any of the following activities to the R.O.:		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d)(7)(i) *Any loss or compromise of his or her keys, passwords, combinations, etc*		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d)(7)(ii) *Any suspicious persons or activities*		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d)(7)(iii) *Any loss or theft of select agents or toxins*		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d)(7)(iv) *Any release of select agents or toxins*		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d)(7)(v) *Any sign that inventory and use records of select agents or toxins have been altered or otherwise compromised*		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(e) Laboratories where select biological agents and toxins are stored or used must be separate from the public areas of the buildings in which they are located.	BMBL BSL-3 and 4 have a separation requirement	All non-exempt labs that possess, use, or transfer select biological agents and toxins

Exhibit 3-1
Summary of New Requirements Resulting in Costs to Affected Entities

(f) When terminating use, an agent must be securely stored, transferred, or destroyed on site		All non-exempt labs that possess, use, or transfer select biological agents and toxins
73.12 Emergency Response		
(a) Develop and implement an emergency response plan for the purpose of protecting public health that meets the requirements under this part	BMBL, p. 227	All non-exempt labs that possess, use, or transfer select biological agents and toxins
(a) Coordinate with and assist emergency respondents in planning for emergencies in various laboratory areas		All non-exempt labs that possess, use, or transfer select biological agents and toxins
73.13 Training		
(a) Provide information and training to persons with approved access and to each unapproved person working in, or visiting, select agent storage and use areas	BMBL, p. 8	All non-exempt labs that possess, use, or transfer select biological agents and toxins
(a) Training must meet all the requirements of this section and ensure that all understand the hazards present in the area		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(b) Provide information and training at the time of initial assignment to work with select agents and prior to assignments involving new exposure situations		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(b) Provide refresher training annually		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d) In lieu of training, the R.O. may certify in writing existing individuals have adequate knowledge, skills, and abilities to carry out duties and responsibilities	BMBL, p. 8	All non-exempt labs that possess, use, or transfer select biological agents and toxins
(e) Ensure each person with access to areas where select agents are stored or handled has received and understood training unless certified under subsection (b)		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(e) Prepare a written record documenting the details of the training (e.g., date and means used to verify employee understood the training)		All non-exempt labs that possess, use, or transfer select biological agents and toxins
73.14 Transfers		
(c) Recipient and sender complete CDC Form EA-101 prior to transfer	72.6(d) of Shipment/Transfer Rule	All non-exempt labs that possess, use, or transfer select biological agents and toxins
(c) Recipient submits CDC Form EA-101 prior to transfer	72.6(d) of Shipment/Transfer Rule	All non-exempt labs that possess, use, or transfer select biological agents and toxins

Exhibit 3-1
Summary of New Requirements Resulting in Costs to Affected Entities

(f) Recipient R.O. provides paper copy or fax of CDC Form EA-101 to sender and to CDC within 2 business days of receipt		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(g) Recipient reports to CDC if the select biological agent or toxin has not been received within 48 hours after the expected delivery time or if the package received had been leaking or otherwise damaged	72.4 of Shipment/Transfer Rule currently says 5 days	All non-exempt labs that possess, use, or transfer select biological agents and toxins
(h) Recipient must report to CDC using a Form EA-101 within 5 business days of the consumption or destruction that occurs after a transfer (Note: N/A when sender and recipient are covered by the same certificate of registration)		All non-exempt labs that possess, use, or transfer select biological agents and toxins
73.15 Records		
The R.O. must maintain the following records:		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(a) Maintain an up-to-date, accurate list of the individual approved for access to select agents and toxins		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(b) Maintain an accurate, current inventory of each select biological agent and toxin held per the requirements under this part		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(c) Maintain records documenting employee access to areas where agents are used or stored and the removal of agents from storage per the requirements under this part		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d) Implement a system to ensure that all records are accurate and authenticity of the records may be verified		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(e) Create a record concerning inspections conducted under 73.10(b)		All non-exempt labs that possess, use, or transfer select biological agents and toxins
(j) Maintain records created and specified under this part for 3 years		All non-exempt labs that possess, use, or transfer select biological agents and toxins
73.16 Inspections		
Allow CDC to inspect the site and records.		All non-exempt labs that possess, use, or transfer select biological agents and toxins

Exhibit 3-1
Summary of New Requirements Resulting in Costs to Affected Entities

73.17 Notification for theft, loss, or release		
(a);(b) Immediately notify CDC (via telephone, fax, or email) and state and local law enforcement upon discovery of a theft or loss (including recovered losses) of a select biological agent or toxin with the info required under this part	72.4 of Shipment/Transfer Rule currently says CDC only	All non-exempt labs that possess, use, or transfer select biological agents and toxins
(d) Immediately notify CDC (via telephone, fax, or email) and state and local public health agencies of any release of a select agent or toxin causing occupational exposure or release outside of the primary containment barriers with the info required under this part	72.3(e) of Shipment/Transfer Rule	All non-exempt labs that possess, use, or transfer select biological agents and toxins
(f) Submit a written follow-up report to CDC (Form 0.1316) within 7 calendar days of theft, loss, or release		All non-exempt labs that possess, use, or transfer select biological agents and toxins
CDC		
73 CDC employees must familiarize themselves with the rule		CDC/USDA
73.6 Exemptions from requirements under this part		
(a)(2) Process and review identification of agents and toxins from telephone calls, faxes, or emails received		CDC/USDA
(a)(7) Process and review Forms 0.1318 sent after a transfer or destruction		CDC/USDA
(c) Process and review application Forms 0.1317 for exemptions (authorized investigations) and provide written decision within 14 days		CDC/USDA
(d) Process and review application Forms 0.1317 for the exemptions due to public health emergency and provide written decision		CDC/USDA
(e) Issue an agricultural emergency exemption, if necessary		CDC/USDA
73.7 Registration		
(b)(1) Issue registration number so that entities may apply for approval under 73.8		CDC/USDA
(b)(2) Process form required by application package		CDC/USDA
(d) Process written notifications of changes to information submitted		CDC/USDA
(e) Process and review applications and issue certificates of registration or amendment		CDC/USDA

Exhibit 3-1
Summary of New Requirements Resulting in Costs to Affected Entities

(g) Process and review applications that have to be re-submitted		CDC/USDA
(g) Issue a certificate of registration or amendment in the event that the entity re-applies		CDC/USDA
(g)(1) Terminate certificate of registration if the recipient no longer conducts activities covered by the certificate		
(g)(2) Terminate a certificate of registration based on failure to comply with regulations or to protect public health and safety.		CDC/USDA
(h) Review notifications to destroy all stocks of a select agent and notify entity. Possibly observe inactivation or take other appropriate action.		CDC/USDA
73.8 Security Risk Assessments		
(f) Process re-applications at least every 5 years		CDC/USDA
(g) For applications requesting an expedited review, CDC must provide a written decision granting or denying the request		CDC/USDA
73.14 Transfers		
(c) Process and review CDC Form EA-101 (pre-transfer) from recipient	72.6(d) of Shipment/Transfer Rule	CDC/USDA
(d) Verify recipient has a certificate of registration		CDC/USDA
(f) Process and review the copy of Form EA-101 (post-transfer) from recipient		CDC/USDA
(g) Address reports in the event that the select biological agent or toxin has not been received within 48 hours after the expected delivery time or if the package received had been leaking or otherwise damaged		CDC/USDA
(h) Process CDC Form EA-101 from recipients when agents are consumed or destroyed (post-transfer) (Note: N/A when sender and recipient are covered by the same certificate of registration)		CDC/USDA
73.16 Inspections		
Conduct inspections of sites and records	72.6(g) of Shipment/Transfer Rule allows for inspections but this is different	CDC/USDA

Exhibit 3-1
Summary of New Requirements Resulting in Costs to Affected Entities

73.17 Notification for theft, loss, or release		
(a);(b) Address notifications of theft or loss	72.4 of Shipment/Transfer Rule currently says CDC only	CDC/USDA
(d) Address notifications of any release of a select agent or toxin that could pose a risk to the public or workers		CDC/USDA
(f) Process the follow-up report Form 0.1316 from entities experiencing a theft, loss, or release		CDC/USDA
ATTORNEY GENERAL		
73 Attorney General must become familiar with the rule		
73.8 Security Risk Assessments		
(d) Conduct risk assessment and notify CDC of any individual who is: (1) A restricted person under 18 U.S.C. 175b, or (2) Reasonably suspected by any Federal law enforcement or intelligence agency of the following: (i) Committing a crime specified in 18 U.S.C. 2332b(g)(5), (ii) Having a knowing involvement with an organization that engages in domestic or international terrorism (as defined in 18 U.S.C. 2331) or with any other organization that engages in intentional crimes of violence, or (iii) Being an agent of a foreign power (as defined in 50 USC 1801).		
(f) Review all clearance requests at least every 5 years in the event that the entity re-applies		

- Does not use recommended practices (assumed equivalent to BSL-1)
- BSL-2
- Combination of BSL-2 and BSL-3
- BSL-3
- BSL-4

- Lab Size. This refers to the size of the lab areas (e.g., area where agents are used, number of staff using agents) as opposed to the size of the organization that owns the lab. Three sizes are modeled:

  - Small
  - Medium
  - Large

Although these variables can be organized into 75 distinct combinations, research suggests that at least 44 of the combinations are infrequent or non-existent. This leaves 31 model facilities, as shown in Exhibit 3-2:

Exhibit 3-2
Summary of Model Facility Types (Non-Exempt)

	BSL-2	*BSL-3*	*BSL-2 & 3*	*BSL-4*	*NRP*
University (10 model facilities)					
Small	●	●	●		
Medium	●	●	●		●
Large	●	●	●		
Government – State/Local (4 model facilities)					
Small					
Medium	●	●	●		●
Large					
Government – Federal (4 model facilities)					
Small					
Medium					
Large	●	●	●	●	
Commercial (9 model facilities)					
Small	●	●	●		
Medium	●	●	●		
Large	●	●	●		
Research Institute (4 model facilities)					
Small					
Medium	●	●	●		
Large				●	

"NRP" indicates non-recommended practices, assumed equivalent to BSL-1.

In addition, a final model facility represents those labs that will be exempt from most of the provisions of the rule but still will incur minor costs to comply with certain transfer and notification requirements and requirements to destroy or transfer select agents within specified time periods. [9]

Although model facilities were selected based on three main characteristics, the full definition of each model also encompasses the following:

- Number of employees with access to select agents
- Number of other employees with access to select agent areas
- Turnover rate
- Number of authorized new employees per year
- Number of entity owners or individuals that control the organization
- Number of times that select agents are accessed per year
- Number of buildings in which select agents are used
- Number of rooms in which select agents are used or stored
- Whether or not toxins are used at the facility
- Number of select agents
- Number of registration amendments per year
- Number of total stock destructions per year
- Number of RO inspections per year
- Whether or not the facility has an existing safety plan
- Whether or not the facility has an inventory tracking system
- Whether or not the facility has a guard at entrance
- Whether or not the facility has an intrusion detection system
- Whether or not the facility has a card key system
- Whether or not the facility has a lock on storage cabinets
- Whether or not the facility has a sign-in/out system
- Whether or not the facility has a risk-based security plan
- Whether or not the facility has a non-risk-based security plan
- Number of times security plan is exercised per year, by type of exercise
- Number of times visitors are on site per year
- Number of security personnel
- Whether or not the facility conducts background checks, by type of check
- Number of employees/year assigned to select agent work for the first time
- Number of transfers per year

[9] These facilities are expected to be covered by the rule's exemption provisions for entities that possess, use, or transfer select agents only as contained in specimens presented for diagnosis, verification, or proficiency testing.

For each model facility, Appendix 2 defines the facility across all of the above characteristics.

3.4 Cost Model

For each model facility, the cost model calculates each of the costs that the facility will incur to alter its facility or practices as needed to comply with each provision of the rule. Appendix 3 identifies the unit costs (including labor rates) used in calculating model facility costs. Appendix 4 reports on the assumed number of hours required by model facilities to complete required activities.

Some costs are one-time costs, some occur periodically (e.g., every five years, whenever certain employees are hired), and some occur annually. For a 20-year timeframe, the cost model assigns appropriate costs to each year, calculates the net present value, and then calculates a level annualized cost.[10] This results in a total annualized cost for each model facility.

The model facility costs are then scaled to a national aggregate annualized cost based on the estimated distribution of labs across the various model facility categories, as shown in Exhibit 3-3.

3.5 Other Assumptions

The methodology makes use of additional assumptions as needed to complete the analysis. The most significant assumptions are as follows:

- The analysis assumes that the minimum physical security measures that will be needed in order to comply with the rule are as follows:

    - All select agent labs: (1) must have and use locked storage cabinets for select agents; (2) must have and use locks on all doors into areas where select agents are used or stored; and (3) must control the distribution of keys to select agent work and storage areas.

    - All BSL-3 labs: (1) must use a card-key system to allow and log entrance into and exit from areas where select agents are used and stored; (2) must station an unarmed security guard at the entrance to each building or floor where select agents are used or stored during working hours; and (3) must use a guard or an intrusion detection system (e.g., motion detectors, sound detectors) during non-working hours.

[10] All calculations involving net present value or annualization assume a seven percent discount rate.

Exhibit 3-3
Assumed Distribution of Labs by Model Facility Type (Non-Exempt)

	BSL-2	*BSL-3*	*BSL-2 & 3*	*BSL-4*	*NRP*
University (285 labs)					
Small	33	28	33		
Medium	33	28	33		49
Large	17	14	17		
Government – State/Local (23 labs)					
Small					
Medium	8	7	8		0
Large					
Government – Federal (75 labs)					
Small					
Medium					
Large	24	24	24	3	
Commercial (375 labs)					
Small	50	50	50		
Medium	50	50	50		
Large	25	25	25		
Research Institute (59 labs)					
Small					
Medium	20	19	19		
Large				1	

"NRP" indicates non-recommended practices, assumed equivalent to BSL-1.
Also, the model facility for exempt clinical/diagnostic facilities is assumed to be representative of 350 labs.

- All BSL-4 labs are assumed to have adequate physical security measures already in place to comply with the rule, although these labs may incur some other security-related costs.

- The analysis calculates costs based on a universe of 1,167 entities that will be affected by the rule. This figure is based on actual notification data, as discussed in Section 2.1.[11] To the extent that there are any affected facilities that did not provide the required notification, or that responded with a false negative, then the analysis will understate the number of affected facilities and the total cost of the rule.

[11] Figures used in the analysis are believed to be current as of October 21, 2002. There may be additional facilities that have been identified since this date that are not reflected in the analysis.

- The rule's exemption provisions (specifically, the exemption for entities that possess, use, or transfer select agents only as contained in specimens presented for diagnosis, verification, or proficiency testing) will be used by all laboratories that conduct only diagnostic work. These entities must comply with certain transfer and notification requirements and must destroy or transfer the select agents within specified time periods, but the entities need not comply with other provisions of the rule.

- The distribution of model facilities is assumed to be as shown in Exhibit 3-3. Although these figures are reasonable based on available information, the actual distribution of labs by size, type, and BSL level is not known.

- The specific characteristics of each model facility, shown in Appendix 2, have been selected based on the research conducted for this study and on other available information described in this report. The composite nature of the model labs makes the selection of specific characteristics a matter of best professional judgment, as available information was not sufficient to define fully all of the models. Many characteristics have been averaged or interpolated based on the available information.

- To obtain clearance under the rule's database review provisions, employees will submit information that is equivalent to the information required to obtain a Government Secret Clearance.

In addition, the analysis reflects a number of other assumptions that are believed to be less significant to the analysis. These smaller assumptions include the following.

Registration

- The registration application and other forms are available on-line.

- The time required to complete a registration application depends in part on the number of select agent labs because some parts of the registration application require information about each area where select agents are used or stored.

- Facilities applying for registration submit their applications via Federal Express.

- All 817 non-exempt facilities register with the CDC in the first year.

- Small facilities submit one amendment every two years, while medium and large facilities submit one and two registration amendments per year, respectively.

Entity & Individual Risk Assessment

- Fifty percent of employees with access to select agent work areas, but not to the select agents themselves, will require background checks and clearance. The other 50 percent are assumed to lose their access to select agent work areas, or are escorted while in select agent work areas.

- For the individual risk assessments, employees will submit information that is equivalent to the information required to obtain a Government Secret Clearance. Fingerprints also are submitted.

- All existing staff that do not currently have a Government Secret Clearance will submit information for a risk assessment.

- All existing staff that currently have a Government Secret Clearance (i.e., staff with access to select agents) will re-submit their information, based on the assumption that these staff received their clearance more than five years prior to the effective date of the rule.

- New staff will submit risk assessment information as they are hired.

- The number of new staff each year is equal to the turnover rate multiplied by the number of staff with access to select agents, rounded up to the nearest whole number.

- All staff with access to select agent areas must undergo a risk assessment and must re-apply every five years.

Safety

- Facilities with existing safety plans will require some time to update the plans to ensure that they meet the standards contained in the rule. The amount of time facilities require to update their existing plans depends on the size of the laboratory facility.

- All current employees with access to select agents will require two hours of safety training to update them on new requirements.

- Facilities that are using practices that are not recommended given the select agents they are handling need to purchase and install one biological safety cabinet for each room in which select agents are handled.

- The RO will conduct two safety inspections per year at BSL-2 facilities, three safety inspections per year at BSL-2-3 and BSL-3 facilities, and four safety inspections per year at BSL-4 facilities.

- The total time required to conduct safety inspections and act on the findings is dependent on the number of lab rooms. For example, larger facilities tend to have more select agents and more lab rooms and thus take longer to inspect than a smaller facility with fewer select agents and one or two lab rooms.

Security

- Only BSL-4 labs currently have a risk based security plan.

- Sixty-two percent of labs have a non-risk based security plan that must be upgraded to meet the requirements in the rule.

- Thirty-eight percent of labs have no security plan.

- The amount of time required to upgrade or develop a security plan is dependent on the size of the facility.

- The amount of time required to review and revise security plans annually is dependent on the size of the facility.

- Only a small number of visitors come to a lab each year and the number of visitors depends on the size of the lab.

- BSL-2 labs require locks on lab doors and storage containers as minimum security requirements.

- BSL-3 labs will employ a guard stationed at the entrance to the building or floor, a card key system, and an after hours intrusion detection system as minimum security requirements. Intrusion detection systems include motion detectors or sound detectors that are remotely monitored.

- Eighteen percent of the BSL-2-3 and BSL-3 labs will install a card key system.

- To ensure that visitors and employees understand the security requirements, they will be given a short security briefing.

- There is no incremental security system implementation cost for facilities that already have an adequate security system in place.

Training

- The duration of initial safety training for those working with select agents is six hours.

- The number of course development hours is eight hours per hour of class time (48 hours) for facilities with no safety plan in place and four hours per hour of class time for facilities with a safety plan.

- The duration of annual refresher training is four hours.

Transfers

- The following activities are not incremental costs because facilities are already conducting these activities: (1) submit Form EA-101 prior to transfer; (2) verify certificates of registration for sender and receiver; and (3) notifying CDC if select agents are not received within 48 hours of when they are expected.

- The number of transfers assumed for each facility varies by the type of entity and the size of the facility.

Records

- The cost to maintain the select agent inventory is dependent on the number of times that biological select agents and toxins are accessed per year and by the number of select agents handled or stored.

- Facilities already maintaining inventory records do not incur incremental costs to maintain their select agent inventory.

- Small facilities handle three select agents. Medium facilities handle 10 select agents. Large facilities handle 20 select agents.

- Facilities are assumed to annually reconcile their select agent inventory records with actual inventory.

- Eighty-five percent of facilities are assumed to have an inventory system in place.

- Eighty-two percent of facilities are assumed to handle toxins.

Notification of Theft, Loss, or Release

- The costs associated with notification of theft, loss, or release are assumed to be immaterial to the analysis due to the low number of thefts, losses, or releases expected per year. These costs are expected to be less than $1,000 per year in aggregate.

3.6 Impacts (including Impacts on Small Entities)

Using industry descriptions under the North American Industry Classification (NAIC) system, the study identified the following seven industries as those that potentially may contain affected labs:[12]

- 325412: Pharmaceutical Preparation Manufacturing
- 325413: In-Vitro Diagnostic Substance Manufacturing
- 325414: Biological Product Manufacturing (except diagnostic)
- 541710: Research and Development in the Physical, Engineering, and Life Sciences
- 611310: Colleges, Universities, and Professional Schools
- 621511: Medical Laboratories
- 622110: General Medical and Surgical Hospitals

These NAICs were then correlated with the relevant model facilities in order to determine the applicable facility costs for firms in different industries. As shown in Exhibit 3-4, each NAIC is assumed to encompass variously-sized labs working at various biosafety levels, with the exception of NAICs 621511 and 622110 which are assumed to encompass those labs that will qualify for exemption from most of the rule (though they still will incur minor costs).

The study then obtained U.S. Economic Census data (1997) for each of these NAICs (except for NAIC 611310[13]). These data included revenue data for NAICs 541710, 621511, and 622110, and value of shipments data for NAICs 325412,

[12] The analysis does not calculate impacts associated with state or federally-owned facilities. Impacts on governments are assumed not to be significant.

[13] Annual revenue figures for colleges, universities, and professional schools have been derived using 1996 data obtained from the National Center for Educational Statistics.

325413, and 325414.[14] For all seven NAICs, the study obtained or derived average values for establishments (or firms) in different size categories (e.g., by number of employees or by range of revenue).[15] These data are presented in Appendix 5.

Exhibit 3-4
Characterization of Labs Used in Different NAICs

NAIC	***Industry Title***	***Type***	***BSL Levels***	***Lab Sizes***
325412	Pharmaceutical Preparation Manufacturing	Commercial	2	Small, Medium, Large
325413	In-Vitro Diagnostic Substance Manufacturing	Commercial	2, 2/3, 3	Small, Medium, Large
325414	Biological Product Manufacturing (except diagnostic)	Commercial	2, 2/3, 3	Small, Medium, Large
541710	Research and Development in Physical, Engineering, and Life Sciences	Research Institute	2, 2/3, 3, 4	Medium, Large
611310	Colleges, Universities, and Professional Schools	University	2, 2/3, 3, NRP	Small, Medium, Large
621511	Medical Laboratories	Exempt	-	-
622110	General Medical and Surgical Hospitals	Exempt	-	-

Note that "Lab Size" refers to the size of the lab operations and not to the size of the entity that owns a lab.
"NRP" indicates non-recommended practices, assumed equivalent to BSL-1.

To determine whether entities that own affected labs will be affected to a significant degree by the rule, the study compares the annual revenue of entities in the relevant industries (including non-profit entities such as some universities and hospitals) to the rule's estimated annualized cost for the appropriate model facilities. Because the rule's cost to affected entities will be highest in the first

[14] Data on value of shipments was collected to serve as a proxy for revenue for the three NAICs within the manufacturing sector because revenue data were unavailable. Although a reasonable proxy (at least for manufacturing firms), value of shipments will understate total revenue because it does not include revenue derived from sources other than manufactured goods (e.g., service revenue, non-operating revenue).

[15] With the exception of the data for NAIC 611310 (colleges and universities), the data analyzed were at the establishment level rather than the firm level. (A single firm may have multiple establishments.)

year in which the rule is effective, this study also considers whether entities may face significant impacts in the first year, even if the annualized impacts are not significant. Entities are assumed not to incur significant impacts unless either or both of the following screening criteria are met:

- The entity's estimated ratio of annualized cost to revenue exceeds one percent.

- The entity's estimated ratio of first-year costs to revenue exceeds three percent.

Entities that meet either of these conditions are subject to additional analysis to determine if they are likely to incur significant impacts as a result of the rule.

Note that these thresholds are intended to serve as screening-level indicators and may be overly sensitive for purposes of identifying economic impacts. For example, to the extent that affected entities may be able to "pass costs through" to their customers, the impact on labs will be reduced. The indicators also may be overly conservative in evaluating first-year impacts based on a threshold of three percent of a *single year's* revenue.

Economic impacts also may be overstated because the analysis uses establishment data as a proxy for firm data and value of shipments as a proxy for revenue. Use of these proxies will tend to understate revenue and, therefore, overstate impacts.

4. Results

This section presents the results of the analysis. Section 4.1 addresses the costs of the rule. Section 4.2 examines the impact of the costs on facilities that operate affected labs. Section 4.3 summarizes the impact results as applicable to small entities affected by the rule.

4.1 Costs

Entities affected by the rule will incur varying costs as they carry out required activities. These activities, which are described in detail in Section 3.2, include registration, background checks, development of safety plans and security plans, security upgrades, and notifications (among others). Most costs will be incurred by the entities owning labs that store and use select agents, though some costs will accrue to CDC as the implementing agency.

4.1.1 Total Cost of the Rule

Based on the analysis described in Section 3, this study estimates the total, annualized cost of the rule at $40 million. Most of this cost will be incurred by affected labs. CDC as the implementing agency will incur somewhat less than $1 million dollars of the annualized total. Because the total annualized cost of the rule is less than $100 million, the rule does not meet the test for an economically significant rule under Executive Order 12866, as discussed in Section 5.1.

4.1.2 Costs to Individual Facilities

Exhibit 4-1 presents the average annualized cost of the rule (across all BSL levels) to non-exempt federal, state, commercial, research institute, and university facilities. Exhibit 4-2 provides additional detail, adding the cost breakout by each BSL level. The median annualized cost of the rule to all non-exempt labs is $29,000, and the range is $9,000-$198,000. In general, costs are highest for labs modeled as having fewer security measures in place prior to the rule. These include BSL-2 labs and university labs.

The average annualized facility cost for exempt clinical/diagnostic labs is estimated at less than $600.

Because much of the rule's cost to affected labs will fall in the first year it is effective, Exhibit 4-3 details first-year costs by facility.

Exhibit 4-1
Average Annualized Cost per Lab,
By Entity Type and Size

Entity Type	**Average Annualized Cost** (Average across applicable BSL levels)		
	Small	**Medium**	**Large**
Federal			$ 25,500
State		$ 16,100	
Commercial	$ 12,000	$ 24,800	$ 35,500
Research Institution		$ 30,400	$ 19,400
University	$ 45,400	$ 113,100	$ 153,400

Exhibit 4-2
Annualized Cost per Lab,
By Entity Type, Size, and BSL Level

Entity Type	**Annualized Cost**				
	Small				
	NRP	BSL-2	BSL-2-3	BSL-3	BSL-4
Federal					
State					
Commercial		$ 16,000	$ 11,000	$ 9,000	
Research Institution					
University		$ 20,000	$ 13,700	$ 102,600	
Entity Type	**Medium**				
	NRP	BSL-2	BSL-2-3	BSL-3	BSL-4
Federal					
State		$ 23,100	$ 21,700	$ 19,600	
Commercial		$ 29,400	$ 23,300	$ 21,900	
Research Institution		$ 31,500	$ 31,100	$ 28,600	
University	$ 67,800	$ 48,600	$ 184,800	$ 151,200	
Entity Type	**Large**				
	NRP	BSL-2	BSL-2-3	BSL-3	BSL-4
Federal		$ 26,900	$ 28,800	$ 28,100	$ 18,100
State					
Commercial		$ 38,300	$ 34,900	$ 33,300	
Research Institution					$ 19,400
University		$ 71,800	$ 197,900	$ 190,400	

"NRP" indicates non-recommended practices, assumed equivalent to BSL-1.

Exhibit 4-3
First Year Cost per Lab,
By Entity Type, Size, and BSL Level

Entity Type	First Year Cost				
	Small				
	NRP	BSL-2	BSL-2-3	BSL-3	BSL-4
Federal					
State					
Commercial		$ 30,700	$ 25,900	$ 23,200	
Research Institution					
University		$ 49,100	$ 40,700	$ 126,400	
Entity Type	**Medium**				
	NRP	BSL-2	BSL-2-3	BSL-3	BSL-4
Federal					
State		$ 75,100	$ 61,400	$ 58,000	
Commercial		$ 64,500	$ 58,600	$ 56,900	
Research Institution		$ 80,900	$ 71,900	$ 57,200	
University	$ 232,200	$ 118,000	$ 729,100	$ 391,200	
Entity Type	**Large**				
	NRP	BSL-2	BSL-2-3	BSL-3	BSL-4
Federal		$ 59,100	$ 61,300	$ 60,000	$ 30,200
State					
Commercial		$ 99,400	$ 77,600	$ 76,200	
Research Institution					$ 36,900
University		$ 174,700	$ 548,100	$ 508,900	

"NRP" indicates non-recommended practices, assumed equivalent to BSL-1.

4.2 Impacts

The analysis calculates impacts, as discussed in Section 3.6, by comparing the annual revenue of firms in the relevant industries to the rule's estimated annualized cost for the appropriate model facilities. Because the rule's cost to affected entities will be highest in the first year in which the rule is effective, the study also considers whether entities may face significant impacts in the first year, even if the annualized impacts are not significant. Firms are assumed not to incur significant impacts unless either or both of the following screening criteria are met:

- The firm's estimated ratio of annualized cost to revenue exceeds one percent.
- The firm's estimated ratio of first-year costs to revenue exceeds three percent.

The results of the analysis are presented separately for affected labs in each industry. Note that these impacts may be mitigated to a significant extent if federal grant money becomes available to pay for required safety and security measures. Many select agent labs operated by states are currently in the process of upgrading safety practices and equipment in conjunction with recent federal grants. Future federal grants are likely to fund similar security upgrades for many select agent labs of all types.

4.2.1 NAIC 325412: Pharmaceutical Preparation Manufacturing

Description

As defined by the US Bureau of the Census, entities in this industry manufacture "*in vivo* diagnostic substances and pharmaceutical preparations (except biological) intended for internal and external consumption in dose forms, such as ampoules, tablets, capsules, vials, ointments, powders, solutions, and suspensions." Firms in this industry qualify as small entities under SBA size standards if they have fewer than 750 employees. An estimated 89 percent of this industry qualifies as small under this definition.

Model Facility Analysis

As manufacturers, firms in this industry fall within the set of model facilities designated as commercial. Lab operations in this industry are assumed to qualify for BSL-2 status because products are intended for human consumption; even at relatively high quantities, BSL-3 status seems unlikely.

The select agent lab facilities at firms in this industry might be small, medium, or large. Note that these size designations refer only to lab operations involving select agents, as opposed to the size of the entity that owns the lab operations. Based on research conducted for this study, the average number of staff with access to select agents ranges from approximately 3-5 for small commercial labs, to approximately 15 for medium commercial labs, and approximately 25 for large commercial labs. Additional staff (that do not use select agents) typically have access to *areas* where select agents are used. These *additional* staff with access to select agent areas are estimated at 3-20 for small labs, 15-30 for medium labs, and 30-50 for large labs. Furthermore, as manufacturing entities, these entities are likely to employ other staff (that do not have access to select agent areas) for other business purposes, such as other manufacturing activities, sales, marketing, personnel, mail services, facilities management, finance and administration, etc. This analysis assumes that there is at least one employee without access to select agent areas for every employee that has access to select agent areas. As a result, the analysis estimates that: (1) each commercial entity owning a small select agent lab has at least 30 employees; (2) each

commercial entity owning a medium select agent lab has at least 75 employees; and (3) each commercial entity owning a large select agent lab has at least 100 employees. These employment ranges are used to evaluate impacts, as discussed below.

Costs and Impacts

The annualized model facility cost for a commercial BSL-2 lab is modeled at $16,000 for a small facility, $29,400 for a medium facility, and $38,300 for a large facility. Under a one-percent cost-to-revenue impact criterion, these entities may incur significant impacts if they have annual revenue of less than $1.6 million (for entities with small labs), $3.0 million (for entities with medium labs), or $3.9 million (for entities with large labs). Based on data from the 1997 Economic Census, however, this study estimates that the average revenue for appropriately-sized firms in this industry (i.e., firms with the same number of employees) exceeds these levels:

- Commercial firms with small select agent labs (at least 30 employees) average an estimated $8.5 million in revenue.

- Commercial firms with medium select agent labs (at least 75 employees) average an estimated $32.0 million in revenue.

- Commercial firms owning large select agent labs (at least 100 employees) earn average revenue substantially in excess of $32.0 million.

Therefore, the rule will not result in significant economic impacts on entities in this industry.

Because the cost of the rule will be highest in the first year in which it is effective, this study also considers whether entities in this industry may incur significant impacts in the first year, even if annualized impacts are not significant. First year model facility costs for a commercial BSL-2 lab are estimated at $30,700 for a small facility, $64,500 for a medium facility, and $99,400 for a large facility. Applying a 3-percent cost-to-revenue impact criterion, this study estimates that the cost of the rule will not result in significant economic impacts on any facilities in this industry.

4.2.2 NAIC 325413: In-Vitro Diagnostic Substance Manufacturing

Description

As defined by the US Bureau of the Census, entities in this industry manufacture “in-vitro (i.e., not taken internally) diagnostic substances, such as chemical,

biological, or radioactive substances. The substances are used for diagnostic tests that are performed in test tubes, petri dishes, machines, and other diagnostic test-type devices." Firms in this industry qualify as small entities under SBA size standards if they have fewer than 500 employees. An estimated 84 percent of this industry qualifies as small under this definition.

Model Facility Analysis

As manufacturers, firms in this industry fall within the set of model facilities designated as commercial. Lab operations in this industry are assumed to include entities operating at BSL-2, BSL-2/3, and BSL-3.

The select agent lab facilities at firms in this industry might be small, medium, or large. Note that these size designations refer only to lab operations involving select agents, as opposed to the size of the entity that owns the lab operations. Based on research conducted for this study, the average number of staff with access to select agents ranges from approximately 3-5 for small commercial labs, to approximately 15 for medium commercial labs, and approximately 25 for large commercial labs. Additional staff (that do not use select agents) typically have access to *areas* where select agents are used. These *additional* staff with access to select agent areas are estimated at 3-20 for small labs, 15-30 for medium labs, and 30-50 for large labs. Furthermore, as manufacturing entities, these entities are likely to employ other staff (that do not have access to select agent areas) for other business purposes, such as other manufacturing activities, sales, marketing, personnel, mail services, facilities management, finance and administration, etc. This analysis assumes that there is at least one employee without access to select agent areas for every employee that has access to select agent areas. As a result, the analysis estimates that: (1) each commercial entity owning a small select agent lab has at least 30 employees; (2) each commercial entity owning a medium select agent lab has at least 75 employees; and (3) each commercial entity owning a large select agent lab has at least 100 employees. These employment ranges are used to evaluate impacts, as discussed below.

Costs and Impacts

The highest annualized model facility costs applicable to this industry are: for small facilities, the commercial BSL-2 lab is modeled at $16,000; for medium facilities, the commercial BSL-2 lab is modeled at $29,400; and for a large facility, the commercial BSL-2 lab is modeled at $38,300. Under a one-percent cost-to-revenue impact criterion, these entities may incur significant impacts if they have annual revenue of less than $1.6 million (for entities with small labs), $3.0 million (for entities with medium labs), or $3.9 million (for entities with large labs). Based on data from the 1997 Economic Census, however, this study

estimates that the average revenue for appropriately-sized firms in this industry (i.e., firms with the same number of employees) exceeds these levels:

- Commercial firms with small select agent labs (at least 30 employees) average an estimated $5.9 million in revenue.

- Commercial firms with medium select agent labs (at least 75 employees) average an estimated $13.0 million in revenue.

- Commercial firms owning large select agent labs (at least 100 employees) earn average revenue substantially in excess of $13.0 million.

Therefore, the rule will not result in significant economic impacts on entities in this industry.

Because the cost of the rule will be highest in the first year in which it is effective, this study also considers whether entities may incur significant impacts in the first year, even if annualized impacts are not significant. First year model facility costs are highest in this industry for small BSL-2 labs ($30,700), medium BSL-2 labs ($64,500), and large BSL-2 labs ($99,400). Applying a 3-percent cost-to-revenue impact criterion, this study estimates that the cost of the rule will not result in significant economic impacts on any facilities in this industry.

4.2.3 NAIC 325414: Biological Product Manufacturing (except diagnostic)

Description

As defined by the US Bureau of the Census, entities in this industry manufacture "vaccines, toxoids, blood fractions, and culture media of plant or animal origin (except diagnostic)." Firms in this industry qualify as small entities under SBA size standards if they have fewer than 500 employees. An estimated 91 percent of this industry qualifies as small under this definition.

Model Facility Analysis

As manufacturers, firms in this industry fall within the set of model facilities designated as commercial. Lab operations in this industry are assumed to include entities operating at BSL-2, BSL-2/3, and BSL-3.

The select agent lab facilities at firms in this industry might be small, medium, or large. Note that these size designations refer only to lab operations involving select agents, as opposed to the size of the entity that owns the lab operations. Based on research conducted for this study, the average number of staff with access to select agents ranges from approximately 3-5 for small commercial

labs, to approximately 15 for medium commercial labs, and approximately 25 for large commercial labs. Additional staff (that do not use select agents) typically have access to *areas* where select agents are used. These *additional* staff with access to select agent areas are estimated at 3-20 for small labs, 15-30 for medium labs, and 30-50 for large labs. Furthermore, as manufacturing entities, these entities are likely to employ other staff (that do not have access to select agent areas) for other business purposes, such as other manufacturing activities, sales, marketing, personnel, mail services, facilities management, finance and administration, etc. This analysis assumes that there is at least one employee without access to select agent areas for every employee that has access to select agent areas. As a result, the analysis estimates that: (1) each commercial entity owning a small select agent lab has at least 30 employees; (2) each commercial entity owning a medium select agent lab has at least 75 employees; and (3) each commercial entity owning a large select agent lab has at least 100 employees. These employment ranges are used to evaluate impacts, as discussed below.

Costs and Impacts

The highest annualized model facility costs applicable to this industry are: for small facilities, the commercial BSL-2 lab is modeled at $16,000; for medium facilities, the commercial BSL-2 lab is modeled at $29,400; and for a large facility, the commercial BSL-2 lab is modeled at $38,300. Under a one-percent cost-to-revenue impact criterion, these entities may incur significant impacts if they have annual revenue of less than $1.6 million (for entities with small labs), $3.0 million (for entities with medium labs), or $3.9 million (for entities with large labs). Based on data from the 1997 Economic Census, however, this study estimates that the average revenue for appropriately-sized firms in this industry (i.e., firms with the same number of employees) exceeds these levels:

- Commercial firms with small select agent labs (at least 30 employees) average an estimated $4.5 million in revenue.

- Commercial firms with medium select agent labs (at least 75 employees) average an estimated $12.1 million in revenue.

- Commercial firms owning large select agent labs (at least 100 employees) earn average revenue substantially in excess of $12.1 million.

Therefore, the rule will not result in significant economic impacts on entities in this industry.

Because the cost of the rule will be highest in the first year in which it is effective, this study also considers whether entities may incur significant impacts in the first year, even if annualized impacts are not significant. First year model facility

costs are highest in this industry for small BSL-2 labs ($30,700), medium BSL-2 labs ($64,500), and large BSL-2 labs ($99,400). Applying a 3-percent cost-to-revenue impact criterion, this study estimates that the cost of the rule will not result in significant economic impacts on any facilities in this industry.

4.2.4 NAIC 541710: Research and Development in the Physical, Engineering, and Life Sciences

Description

As defined by the US Bureau of the Census, this industry category "comprises establishments primarily engaged in conducting research and experimental development in the physical, engineering, or life sciences, such as agriculture, electronics, environmental, biology, botany, biotechnology, computers, chemistry, food, fisheries, forests, geology, health, mathematics, medicine, oceanography, pharmacy, physics, veterinary, and other allied subjects." Entities in this NAIC may operate either as for-profit entities or not-for-profit entities. In either case, they qualify as small entities under SBA size standards if they have fewer than 500 employees. An estimated 97 percent of this industry qualifies as small under this definition.

Model Facility Analysis

Select agent labs within this industry are mapped to the research institute model facilities. Lab operations in this industry are assumed to include medium-sized labs operating at BSL-2, BSL-2/3, and BSL-3, and one large lab operating at BSL-4. Note that these size designations refer only to lab operations involving select agents, as opposed to the size of the entity that owns the lab operations.

Based on research conducted for this study, the number of staff with access to select agents ranges from approximately 20-30 for medium labs. Additional staff (that do not use select agents) typically have access to *areas* where select agents are used. These *additional* staff with access to select agent areas are estimated at 5-50 for medium research institute labs. Furthermore, these entities employ additional staff for other purposes (e.g., other research activity, fundraising, personnel, and administration). Based on research conducted for this study, the analysis estimates that: (1) each research institute owning a medium select agent lab employs at least 50 employees; and (2) each research institute owning a large select agent lab employs at least 50 employees.

Costs and Impacts

The highest annualized model facility costs applicable to this industry are: for medium facilities, the research institute BSL-2 lab is modeled at $31,500; and for

a large facility, the research institute BSL-4 lab is modeled at $19,400.[16] Under a one-percent cost-to-revenue impact criterion, these entities may incur significant impacts if they have annual revenue of less than $3.2 million (for entities with medium labs), or $2 million (for entities with large labs). Based on data from the 1997 Economic Census, however, this study estimates that the average revenue for appropriately-sized firms in this industry (i.e., firms with the same number of employees) exceeds these levels:

- Research institutes with medium *or* large select agent labs (at least 50 employees) average an estimated $6.5 million in revenue.

Therefore, the rule will not result in significant economic impacts on entities in this industry.

Because the cost of the rule will be highest in the first year in which it is effective, this study also considers whether entities may incur significant impacts in the first year, even if annualized impacts are not significant. First year model facility costs are highest for medium BSL-2 labs ($80,900), and large BSL-4 labs ($36,900). Applying a 3-percent cost-to-revenue impact criterion, this study estimates that the cost of the rule will not result in significant economic impacts on any facilities in this industry.

4.2.5 NAIC 611310: Colleges, Universities, and Professional Schools

Description

As defined by the US Bureau of the Census, this industry category includes "establishments primarily engaged in furnishing academic courses and granting degrees at baccalaureate or graduate levels. The requirement for admission is at least a high school diploma or equivalent general academic training." Entities in this NAIC may operate either as for-profit entities or not-for-profit entities. In either case, they qualify as small entities under SBA size standards if they have annual revenue of less than $6 million. Approximately 11 percent of colleges and universities qualify as small under this definition.

Model Facility Analysis

Select agent labs within this industry are mapped to the university model facilities. Lab operations in this industry are assumed to include entities operating at BSL-2, BSL-2/3, BSL-3, as well as some labs that should be at BSL-2 but are using non-recommended practices. The select agent lab facilities at

[16] BSL-4 facilities are assumed to require the fewest changes to meet the rule's safety and security requirements.

universities might be small, medium, or large. Note that these size designations refer only to lab operations involving select agents, as opposed to the size of the entity that owns the lab operations.

The analysis assumes that universities with select agent labs are among those that are known for their commitment to conducting scientific research. Academic institutions that conduct the most scientific research generally are larger than other colleges and universities. Consequently, this study assumes that the smallest colleges and universities are unlikely to own select agent labs. As a minimum threshold, the analysis assumes that colleges and universities with annual revenue of less than $30 million are unlikely to own select agent labs. As shown in Exhibit 4-4, colleges and universities with annual revenue of less than of $30 million are quite small, judging by scientific research standards. It is likely that the typical annual revenue for universities that own select agent labs is substantially higher than $30 million.

Costs and Impacts

The highest annualized model facility costs applicable to universities are: for small facilities, the BSL-3 lab is modeled at $102,600; for medium facilities, the BSL-2/3 lab is modeled at $184,800; and for a large facility, the BSL-2/3 lab is modeled at $197,900. Under a one-percent cost-to-revenue impact criterion, universities that own these labs may incur significant impacts if they have annual revenue of less than $10.3 million (for entities with small labs), $18.5 million (for entities with medium labs), or $19.8 million (for entities with large labs). Using the $30 million minimum annual revenue figure described in the preceding paragraph, this study estimates that the average revenue for appropriate universities exceeds these levels and, therefore, that the rule will not result in significant economic impacts on universities.

Because the cost of the rule will be highest in the first year in which it is effective, this study also considers whether universities may incur significant impacts in the first year, even if annualized impacts are not significant. First year model facility costs are highest for small BSL-3 labs ($126,400), medium BSL-2/3 labs ($729,100), and large BSL-2/3 labs ($548,100). Applying a 3-percent cost-to-revenue impact criterion, universities that own these labs may incur significant impacts if they have annual revenue of less than $4.3 million (for entities with small labs), $24.4 million (for entities with medium labs), or $18.3 million (for entities with large labs). Using the $30 million minimum annual revenue figure

Exhibit 4-4
Sample of Colleges and Universities at Various Revenue Thresholds

$6 – $15 Million Annual Revenue

- Colorado Technical University
- Lancaster Bible College (PA)
- Indiana Institute of Technology (IN)
- Alaska Pacific University
- Naropa University (CO)
- Bethany College (KS)
- Pikeville College (KY)
- Union College (KY)
- Husson College (ME)
- Lasell College (MA)

$15 – $30 Million Annual Revenue

- Harvey Mudd College (CA)
- Lynn University (FL)
- Coe College (IA)
- St. John's College (MD)
- Hastings College (NE)
- Hampden-Sydney College (VA)
- Mary Baldwin College (VA)
- Sweet Briar College (VA)
- Randolph-Macon College (VA)
- Guilford College (NC)

$30 – $50 Million Annual Revenue

- Spelman College (GA)
- Cornell College (IA)
- Luther College (IA)
- Hampshire College (MA)
- Kalamazoo College (MI)
- Kenyon College (OH)
- Mary Washington College (VA)
- Wheeling Jesuit University (WV)
- Haverford College (PA)
- Reed College (OR)

$50 – $75 Million Annual Revenue

- Pomona College (CA)
- Butler University (IN)
- Bowdoin College (ME)
- Amherst College (MA)
- Carleton College (MN)
- Macalester College (MN)
- Davidson College (NC)
- Dickinson College (PA)
- Washington and Lee University (VA)
- Swarthmore College (PA

$75 – $100 Million Annual Revenue

- Drake University (IA)
- Mount Holyoke College (MA)
- Williams College (MA)
- Colgate University (NY)
- Vassar College (NY)
- Middlebury College (VT)
- Loyola College (MD)
- Saint Olaf College (MN)
- Oberlin College (OH)
- Radford University (VA)

$100 – $250 Million Annual Revenue

- Wesleyan University (CT)
- American University (DC)
- Smith College (MA)
- New York Medical College (NY)
- Miami University – Oxford (OH)
- Bryn Mawr College (PA)
- Bucknell University (PA)
- Rice University (TX)
- James Madison University (VA)
- Marquette University (WI)

$250 – $500 Million Annual Revenue

- Florida State University (FL)
- University of Notre Dame (IN)
- Boston College (MA)
- Dartmouth College (MA)
- Syracuse University (NY)
- Wake Forest University (NC)
- Carnegie Mellon University (PA)
- Brown University (RI)
- Clemson University (SC)
- George Mason University (VA)

$500 Million + Annual Revenue

- Yale University (CT)
- University of California Berkely (CA)
- Indiana University (IN)
- University of Minnesota (MN)
- University of Michigan (MI)
- University of North Carolina (NC)
- Pennsylvania State University (PA)
- Texas A & M University (TX)
- University of Virginia (VA)
- University of Wisconsin (WI)

described above, this study estimates that the average revenue for appropriate universities exceeds these levels and, therefore, that the first-year costs of the rule will not result in significant economic impacts on universities.

4.2.6 NAIC 621511: Medical Laboratories

Description

As defined by the US Bureau of the Census, this industry category includes "establishments known as medical laboratories primarily engaged in providing analytic or diagnostic services, including body fluid analysis, generally to the medical profession or to the patient on referral from a health practitioner." Firms in this industry qualify as small entities under SBA size standards if they have annual revenue of less than $11.5 million. An estimated 92 percent of this industry qualifies as small under this definition.

Model Facility Analysis

Select agent labs within this industry are expected to be covered by the rule's exemption provisions for entities that possess, use, or transfer select agents only as contained in specimens presented for diagnosis, verification, or proficiency testing. The average annualized cost to these facilities is less than $600. Under a one-percent cost-to-revenue impact criterion, medical laboratories that own these labs may incur significant impacts if they have annual revenue of less than $60,000. However, the average annual revenue for medical laboratories with as few as 0-5 employees exceeds $300,000. Therefore, this study estimates that these facilities will not face significant economic impacts as a result of the rule.

4.2.7 NAIC 622110: General Medical and Surgical Hospitals

Description

As defined by the US Bureau of the Census, this industry category includes "establishments known and licensed as general medical and surgical hospitals primarily engaged in providing diagnostic and medical treatment (both surgical and nonsurgical) to inpatients with any of a wide variety of medical conditions. These establishments maintain inpatient beds and provide patients with food services that meet their nutritional requirements. These hospitals have an organized staff of physicians and other medical staff to provide patient care services. These establishments usually provide other services, such as outpatient services, anatomical pathology services, diagnostic X-ray services, clinical laboratory services, operating room services for a variety of procedures, and pharmacy services." Entities in this NAIC may operate either as for-profit entities or not-for-profit entities. In either case, they qualify as small entities

under SBA size standards if they have annual revenue of less than $29 million. An estimated 51 percent of this industry qualifies as small under this definition.

Model Facility Analysis

Many select agent labs within this industry are expected to be covered by the rule's exemption provisions for entities that possess, use, or transfer select agents only as contained in specimens presented for diagnosis, verification, or proficiency testing. The average annualized cost to these facilities is less than $600. Under a one-percent cost-to-revenue impact criterion, hospitals that own these labs may incur significant impacts if they have annual revenue of less than $60,000. However, the average annual revenue for even the smallest hospitals (those with 10-19 employees) exceeds $1.2 million. Therefore, this study estimates that these facilities will not face significant economic impacts as a result of the rule.

Hospitals that are not exempt are assumed to be teaching hospitals associated with universities; therefore, impacts on these non-exempt hospitals are among those discussed in Section 4.2.5.

4.3 Small Entity Impacts

As discussed in detail in the preceding section, the rule is not expected to result in significant impacts on any entities that are affected by the rule, including small entities affected be the rule. Although many of the 817 affected select agent labs (other than the university labs) are likely owned by entities that qualify as small under SBA size standards, even these small entities are large enough so that the impacts of the rule will not qualify as substantial.

5. Required Regulatory Analyses

5.1 Economic Impact Analysis

Under Executive Order 12866 (58 FR 51735, October 4, 1993), federal agencies must determine whether a regulatory action is "significant" and, therefore, subject to OMB review and the requirements of the Executive Order. The Order defines "significant regulatory action" as one that is likely to result in a rule that may:

(1) Have an annual effect on the economy of $100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or state, local, or tribal government or communities.

(2) Create a serious inconsistency or otherwise interfere with an action taken or planned by another agency.

(3) Materially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof.

(4) Raise novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in the Executive Order.

Although this rule does not meet the test for an economically significant rule, as addressed in Section 4.1.1, HHS has determined that the rule is significant because it imposes requirements on entities that had not previously been subject to regulation in this area. In addition, the requirements for security at labs and government approval of staff are new and will significantly change practices at some entities and could affect staffing. Consequently, as required under the E.O. 12866 section 6(A)(3)(B)(ii), HHS conducted an analysis of the costs and benefits of the rule. This analysis is presented in the preceding chapters of this document.

5.2 Federalism Analysis

Executive Order 13132 of August 4, 1999, "Federalism," requires agencies to identify policies that have federalism implications and to adhere to certain specified criteria when formulating and implementing policies that have federalism implications. "Policies that have federalism implications" are defined as, *inter alia,* regulations, policy statements, or other actions "that have

substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government."

Promulgation of the interim final rule on select biological agents and toxins does not appear to meet the criteria specified for a policy that has federalism implications. This conclusion is based on the following analysis:

(1) Neither the relationship between the States and the national government nor the distribution of powers and responsibilities among the various levels of government are affected by the requirements regarding the possession and use in the United States and the transfer into or within the United States of select biological agents and toxins.

(2) The requirements may have a relatively slight, if secondary, effect on certain States as a result of actions that will be required to be taken by laboratories at State-run universities. Also, States may be directly affected as a result of actions that will be required to be taken by facilities operated by State agencies, such as pathology laboratories operated by State Departments of Health. However, these actions are unlikely to create "substantial direct effects on the States." The actions, and their potential effects on States, include the following:

- Registration. Under the interim final regulation, an entity may not possess or use in the United States, or transfer into or within the United States, any select biological agent or toxin unless the entity has been granted a certificate of registration. State-run entities will be required to prepare registration application packages. However, entities that satisfy the requirements for exemption from registration will be required only to make certain reports of transfer or destruction of the select biological agents and toxins. Facilities operated by State agencies can be expected in many cases to qualify for exemption.

- Submission of Entity Information for Review by the Attorney General. State agencies are expressly exempted from this requirement.

- Submission of Individual Information for Review by the Attorney General. All entities, including State entities, will be required to submit information about individuals who would have access to a select biological agent or toxin so that the individual can be approved or denied approval for access. However, information is not required to be supplied for individuals at entities that are exempt from the registration requirement. Thus, facilities operated by State agencies that qualify for exemption also will not be affected by this requirement.

- Designation of Responsible Official, Preparation of Safety Plan, Security Plan, and Emergency Response Plan, and Training for Individuals. Each entity, including State entities, registered to possess, use, or transfer a select biological agent or toxin is required by the regulation to identify and authorize an individual as a Responsible Official to ensure that the entity meets the regulatory requirements; to develop and implement a safety plan for ensuring biosafety standards and requirements are met; to develop and implement a security plan to ensure the security of laboratories containing select biological agents and toxins; to develop and implement an emergency response plan for the purpose of protecting public health; and to provide information and training to each person with access to areas where select biological agents and toxins are handled or stored. However, these activities are not required to be performed by entities that are exempt from the registration requirement. Thus, facilities operated by State agencies that qualify for exemption will also not be affected by these requirements.

- Notices and Records of Transfers, Theft, Loss, or Release. Entities, including entities exempt from registration, may not transfer select biological agents or toxins without submitting, prior to the transfer, a CDC Form EA-101. The form must be signed by the ROs for both the sender and the recipient (when both are registered). When the sender is not a registered entity, the form must be signed by the individual with authority for ensuring compliance with the regulatory requirements. All senders must report in-transit losses. Any release of a select agent or toxin that could pose a risk to the public or workers must be reported. Registered entities must provide notice of theft or loss of a select biological agent or toxin. Thus, State entities will be required to make certain notices and records.

Even if the effects on the States described above are determined to be "substantial direct effects," the policies being adopted in the interim final rule satisfy the Federalism Policymaking Criteria outlined in EO 13132: (a) To the extent that the policymaking discretion of the States is limited by the interim final rule, the necessity for such action arises from a Federal statute mandating the promulgation of regulations; (b) Congress has determined that national action is appropriate in light of the presence of a problem of national significance. That problem is the threat posed by select agents and toxins to public health and safety, and the need to improve the ability of the United States to prevent, prepare for, and respond to bioterrorism and other public health emergencies; (c) The interim final rule does not create intrusive Federal oversight of State administration; (d) Congress has specified by statute that uniform national standards are required. However, the interim final rule does not preempt existing State law, and when appropriate, State officials have been consulted in development of the standards.

5.3 Taking of Private Property Analysis

Executive Order 12630 of March 15, 1988, "Government Actions and Interference With Constitutionally Protected Property Rights," requires Federal agencies to review their regulatory actions to prevent unnecessary "takings" of private property for public use and to account in their decision-making for those takings that are necessitated by statutory mandate. "Policies that have takings implications" are defined as "rules and regulations that propose or implement licensing, permitting, or other condition requirements or limitations on private property use, or that require dedications or exactions from owners of private property."

The rule on select biological agents and toxins has, at most, very minor takings implications. It does not constitute an action that will result in a physical invasion or occupancy of private property. The requirements will not lead to a "complete deprivation of all use or value" and are not likely even to "substantially affect" the value or use of private property, even temporarily. Furthermore, as the Executive Order notes, actions taken specifically for the purpose of protecting public health and safety are ordinarily given broader latitude before being considered as takings, and the stated Congressional purpose of the requirements on select biological agents and toxins is to ensure the safety and security of the American people.

The requirements address the possession, use, and transfer of select biological agents and toxins. Thus, the requirements address private property only to the extent that the use of certain facilities where agents and toxins might be stored, used, or transferred may be affected. The effects, if any, will arise from the requirement that the entities operating those facilities be registered and that those entities adopt safety plans and security plans that may require physical changes to their facilities. However, the requirements meet the criteria stated by EO 12630:

- Restrictions imposed on the use are not disproportionate to the extent to which the use could contribute to the overall problem. The interim final rule allows exemptions and, for those entities that are not exempt, safety and security plans may, within specified limits, be tailored to the entity's particular situation;

- The duration of the registration process will be kept to the minimum necessary;

- The public health or safety risk is clearly and specifically identified; and

- The interim final rule will substantially advance the purpose of protecting public health and safety against the specifically identified risk.

5.4 Evaluation of the Need for Civil Justice Reform Analysis

Executive Order 12988 of February 5, 1996, "Civil Justice Reform," requires Federal agencies that conduct or otherwise participate in civil litigation on behalf of the United States Government in Federal court to adhere to guidelines specified in the Executive Order during the conduct of such litigation. Because the interim final regulation does not involve civil litigation on behalf of the United States Government, none of the actions called for by the Executive Order with respect to such litigation are necessary.

Executive Order 12988 also requires each agency promulgating new regulations to ensure that the regulations have been reviewed to eliminate drafting errors and ambiguity, are written to minimize litigation, and provide a clear legal standard. The Executive Order requires an agency formulating regulations to make every reasonable effort to ensure that the regulation, as appropriate:

- specifies in clear language the preemptive effect, if any, to be given the regulation;

- specifies the effect on existing Federal law or regulation, if any, including all provisions repealed, circumscribed, displaced, impaired, or modified;

- provides a clear legal standard for affected conduct rather than a general standard, while promoting simplification and burden reduction;

- specifies in clear language the retroactive effect, if any, to be given to the regulation;

- specifies whether administrative proceedings are to be required before parties may file suit in court and, if so, describes those proceedings and requires the exhaustion of administrative remedies;

- defines key terms, either explicitly or by reference to other regulations or statutes that explicitly define those items; and

- addresses other important issues affecting clarity and general draftsmanship of regulations set forth by the Attorney General.

The interim final regulation on select biological agents and toxins has no preemptive effect; specifies its relationship to the provisions of other laws; incorporates clear legal standards; has no retroactive effect and specifies when,

in the future, its provisions become effective; specifies administrative proceedings for appeal of adverse decisions under the rule; provides for civil penalties as specified under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002; and defines key terms. Therefore, no additional analysis or actions are required under EO 12988.

5.5 Protection of Children Analysis

Executive Order 13045 of April 21, 1997, "Protection of Children From Environmental Health Risks and Safety Risks," requires each Federal agency to ensure that its policies, programs, activities, and standards address disproportionate risks to children that result from environmental health risks or safety risks. The Executive Order requires an evaluation of the environmental health or safety effects of a planned regulation on children if the regulation is economically significant and concerns an environmental health risk or safety risk that the agency has reason to believe may disproportionately affect children.

The regulation on select biological agents and toxins is neither economically significant nor is it known to involve a safety risk likely to disproportionately affect children. Some select biological agents and toxins may pose a greater risk to children than to healthy adults. Generally, however, aged and immuno-compromised adults have been identified as being at greater risk.

The biosafety and security plans that must be developed and implemented by entities registered to possess, use, receive, or transfer select biological agents and toxins will protect children from exposure to the agents and toxins, either within the buildings and rooms where the select biological agents and toxins will be stored or used, or as a consequence of accidental or deliberate release. Children would be expected to be completely barred from access to facilities where the select biological agents are stored or used by the requirement that an entity obtain approval, following an individual database review, for every individual given access. Therefore, no additional protection of children analysis is required.

5.6 Indian Tribal Government Analysis

Executive Order 13175 of November 6, 2000, "Consultation and Coordination With Indian Tribal Governments," requires agencies that develop Federal policies with tribal implications to consult with tribal government officials, encourage tribes to develop their own standards, and defer to such tribal standards. The regulation on biological agents and toxins, however, is not an action that will have "substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes."

Therefore, no additional consultation and coordination with Indian tribal governments is necessary.

5.7 Energy Effects Analysis

Executive Order 13211 of May 18, 2001, "Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use," requires agencies to prepare a "Statement of Energy Effects" for proposed government regulatory actions that "significantly affect the supply, distribution, and use of energy." The regulation on biological agents and toxins will not be a significant energy action. In particular, it will not be a significant regulatory action under Executive Order 12866 nor is it "likely to have a significant adverse effect on the supply, distribution, or use of energy," which the Executive Order also describes as including a shortfall in supply, price increases, or increased use of foreign supplies should the proposal be implemented. Therefore, no Statement of Energy Effects is required.

5.8 NEPA Assessment

The National Environmental Policy Act (NEPA), as amended, (42 USC 4321-4347) requires, for "major Federal actions significantly affecting the quality of the human environment": a detailed statement on the environmental impact of the proposed action; any adverse environmental effects that cannot be avoided if the proposal is implemented; alternatives to the proposed action; the relationship between local short-term uses of the environment and the maintenance and enhancement of long-term productivity; and any irreversible and irretrievable commitments of resources which would be involved in the proposed action should it be implemented.

The interim final rule on select biological agents and toxins, if adopted, would not be a major Federal action significantly affecting the quality of the human environment and, therefore, an environmental impact statement is not required. The rule will not have any significant environmental impact for the following reasons:

- The rule is primarily procedural in nature, addressing the registration of entities and individuals for the possession, use, receipt, or transfer within the United States of select biological agents or toxins. It requires submission of information and the development of safety plans and security plans.

- The implementation of safety plans and security plans, both of which are required by the rule, may involve commitments of resources by entities. However, significant components of the implementation will be procedural,

involving training, escorts and monitoring, reporting, recordkeeping, inspections, procedures for access control, and emergency response. These activities will have no environmental impact and will require minimal commitment of resources.

- The actions required by the interim final rule are generally specifically mandated by statute. To the extent that actions are not specifically mandated by statute, the CDC has reviewed alternatives and has not identified alternatives that would achieve the goals of the statute with a lesser impact on the environment than the alternatives selected.

5.9 Need for Unfunded Mandates Analysis

The Unfunded Mandates Reform Act (UMRA) of 1995 (Public Law 104-4, 2 USC 1501 et seq.) requires a Federal agency to assess the effects of its regulatory actions on State, local, and tribal governments and the private sector. Before promulgating any notice of proposed rulemaking for a rule "that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any 1 year..." the agency must prepare, among other things, a "qualitative and quantitative assessment of the anticipated costs and benefits of the Federal mandate." (2 U.S.C. 1532)

Because the proposed rule on select biological agents and toxins is not a "significant" regulatory action, defined by UMRA as resulting in aggregate expenditures in one year of $100 million or more, no additional UMRA analysis is required.